

Nature in the Future

It ill becomes a journal to waste too much of its space on introspection, as John Maddox stressed in his last editorial (May 18 of this year). In the long run, *Nature* will prosper or not on the strength of its actual, not its avowed, editorial policy. Nevertheless, a new Editor may be excused a little public musing on what he sees for *Nature* if only because of the intimacy that exists between the journal and its readership and to which Mr Maddox alluded. Many of *Nature's* regular readers would expect a new Editor to explain himself though none should require him to show all his cards nor to deliver all his promises in the too-immediate future.

It is the quality of the papers submitted to *Nature* which ultimately controls its success or failure. Good as one hopes the journal will be from beginning to end, it is clear that a stream of second-rate scientific papers would be the quickest road to oblivion. Thus an Editor's first responsibility is to ensure that the standard of papers is high. This is, of course, a task which it would be impossible to perform without a diligent staff and a small army of patient reviewers, but at the centre of it lies the editorial question—"Is it a *Nature* paper?" No two people would agree on the definition of a *Nature* paper, but some common ground is clear. Many a thoroughly correct and readable manuscript has to be declined for lack of something which sets it apart as helping to see the world through a newer and better window. On the other hand room has to be found for the speculative paper in which cast-iron evidence cannot be adduced but which has the potential to open up new fields of research.

Two specific points should be made concerning scientific papers. The first is one of growing concern to all connected with the production of the journal—brevity. In *Nature's* centenary number (November 1, 1969) a few of the journal's most exciting papers were reprinted. It was something of a surprise to find that in the 1930's the Cockcroft-Walton generator could be announced in less than 300 words and the fission of uranium postulated in less than a page. Brevity was not confined to the physicist. In 1953, the structure of DNA was announced in one page. With some justification one can argue that science is now bigger, techniques are more complex, and so on. Yet *Nature* simply cannot in the foreseeable future expand to accommodate longer papers, nor is it all clear that readers would wish us to do so. Scientists-as-readers seem to demand more brevity than scientists-as-writers are prepared to give.

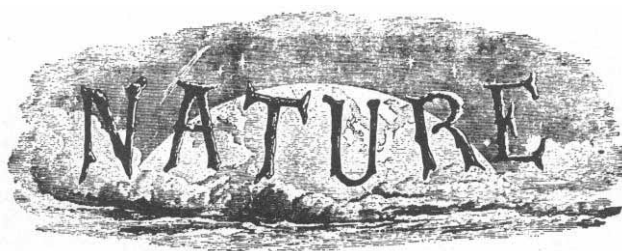
The second point is a personal dislike for papers in which all bets are hedged. A. J. Leibling, a highly perceptive observer of the press, used to write of the "ademonai-kodemonai" (Japanese for "on-the-one-hand-this-on-the-other-hand-that") syndrome amongst journalists with lots of possibilities to juggle stemming from one hard but at present uninterpretable fact. Americans will recognize this syndrome amongst their political commen-

tators. We would rather carry the simple observation unadorned than have it smothered in unhelpful ademonai-kodemonai.

Reassurance ought to be given to those who view the change to one *Nature* per week in January 1974, announced recently, as reflecting some radical switch in editorial policy. This is not so. Many ingredients of course have gone into the making of this decision and the editorial view is only one of them. But it has been clear after many conversations with contributors and readers that there was a preference for a unified weekly. The amount of space for contributions will remain roughly the same as that which is now available in the three journals.

Scientific papers are our bread and butter, but it will be obvious that the amount and quality of the jam has also improved over the past few years in coverage and exposition of science and its news and politics. The aim will be to increase the scope of these sections and to prevent their developing into bland reporting. Fine words, but what do they mean in practice? *Nature's* news gathering facilities around the world must grow in the next year or two, as it is increasingly necessary to understand the scientific scene away from the trans-Atlantic axis. Furthermore, *Nature* must be an open journal, reflecting the sense of community which is still very strong amongst scientists. In the long run much of *Nature* is simply scientists talking to scientists about things which have a broad interest. Opinions differ about what constitutes "broad interest" and we can make no claim that the exposition and opinion sections of the journal give a uniform and totally balanced coverage. But the remedy to that is in the hands of readers. If you think there is more to tell or another side to a story, let us hear it.

100 Years Ago



A day will come when every great Administration will have its Consulting Committee, composed almost exclusively of men of science, and then many mistakes will be avoided, and many forces utilised which are at present lost. But in order that such an institution should be born and developed, it is necessary that the function of Science be universally comprehended and accepted. To attain this result is one of the chief aims of the French Association.

From *Nature* 8, 349, August 24, 1873



OLD WORLD

Dr Zhores Medvedev Replies to Professor John Ziman

DEAR PROFESSOR ZIMAN,

I have read your "Second Letter to an Imaginary Soviet Scientist" with great interest (*Nature*, 243, 489; 1973). I doubt whether you have received many replies from the USSR. As you probably remember, your first letter (*Nature*, 217, 123; 1968) did not induce many replies either. My own reply sent to you in April 1968 started our correspondence and friendship, and I explained to you then that in the photocopied version of *Nature* which was available in the USSR your letter was not reproduced at all so that only a few scientists in the USSR have known of your appeal. I can add now that even though the USSR has signed the Universal Copyright Convention, which does not permit the distribution of photocopies of *Nature*, your second letter has also only been seen by few people in the USSR because this page was simply cut out from the copies of *Nature* in Soviet libraries.

As you know I was officially invited to Britain in January, but a few weeks ago the Soviet authorities unexpectedly deprived me of my citizenship, a decision made partly on the basis that according to them the invitation was private. But I assure you that I had thought of answering your letter before this unhappy development—at a time when I was legally one of those to whom you addressed your letter.

In your second letter you asked us to say whether the boycott of conferences and symposia in the USSR would help those Soviet scientists whose human rights are being violated. You are right to say that there is no simple answer and that, in general, the boycott of scientific meetings is not a good way to help those who are in trouble. I am sure that the isolation of the Soviet scientific community does not help Soviet scientists. During recent years, in spite of many troubles at home, I was usually very glad to meet foreign colleagues in the USSR. These meetings gave me great moral support and they had a significant influence on my research work. But when you arrive in the USSR there are several approaches you can take. You can, for example, ignore the official ceremony and have private meetings with friends or colleagues whom you like and want to support. But, of course, if you find that such friendly contacts with individuals are impossible because of interference from bureaucrats or the police, then you certainly have to make a protest or return home.

But the situation which faces foreign scientists could be more complex than that. I give you one such example.

The World Psychiatric Association will hold an international symposium on "Aspects of Schizophrenia" in the USSR next October. The Soviet hosts have selected two very attractive Caucasus cities. Two days of meetings will take place in Yerevan and two others in Tbilisi. The ministers of health of both republics, Armenia and Georgia, will give opening addresses. Armenians and Georgians are very nice and traditionally open and hospitable people. I am sure that British, French and other foreign participants at this symposium will have a very good time.

But there are other problems which cannot be ignored. Among the speakers are A. V. Snezhnevsky, G. Morosov and R. A. Nadzharov who were responsible for many decisions which sent some political "dissidents" into psychiatric prison-hospitals. Two scientists, Dr Leonid Plyshch and Yuri Shikhanovitch, have been their most recent victims. You probably remember that the same three psychiatrists examined me in 1970 and the methods of their "work" have been described in the book *Question of Madness* written by my brother and I. There have been several other protests about abuses of psychiatry in the USSR and the forthcoming symposium with

these three "heroes" of many well-known psychiatric-political cases present is a unique chance for western scientists to investigate these accusations at first hand.

I do not suggest that western scientists try and obtain first hand knowledge of some political "patients", for they will not be allowed to do so. I am sure that A. Snezhnevsky and G. Morosov will always be able to produce for foreign observation some clear mental syndromes even in local Caucasus clinics. But there is a more general aspect of the problem which honest scientists cannot ignore.

On August 8, 1973, Professor R. Nadzharov distributed through Tass a statement which said that suggestions about the use of psychiatry to punish "different-minded people . . . are a part of an anti-Soviet propaganda campaign launched by hired professional anti-Sovietists". Professor Nadzharov explained that "... the Soviet laws in this field are in principle similar to the laws operating in most other countries and that the Soviet laws specifically provide legal punishment for the persons guilty of unjustified placing of the patient in a mental hospital". Nadzharov noted that all slanders about abuses of psychiatry in the USSR had been rejected by the World Association of Psychiatry. That the world association has in the past

Conference On Aspects of Schizophrenia

ACCORDING to the preliminary announcement of the International Conference on Aspects of Schizophrenia to be held in Yerevan and Tbilisi in the Soviet Union from October 8 to October 12, 1973 the following are to be present:

H. P. Rome (USA), A. V. Snezhnevsky (USSR), S. Follin (France), A. Megrabyan (USSR), H. Rennert (East Germany), G. Morosov (USSR), J. J. López Ibor (Spain), R. A. Nadzharov (USSR), L. Eisenberg (USA), C. Koupernik (France), M. Vrono (USSR), V. Bashina (USSR), R. de la Fuente (Mexico), E. Strömberg (Denmark), J. K. Wing (Britain), H. Collomb (Senegal), Z. Serebryakova (USSR), G. Hunter (FRG), Z. Zharikov (USSR), K. Heinrich (West Germany), R. F. Prien (USA), M. H.

Lader (Britain), P. C. Baastrup (Denmark), A. Smulevitch (USSR), R. Gardner (Britain), Yu. Saarma (USSR), W. Linford Rees (Britain), A. Zurabashvili (USSR), A. J. Coppen (Britain), I. Yamashita (Japan), A. J. Mandell (USA), J. M. Davis (USA), A. Freedman (USA), C. E. Frohman (USA), R. Lideman (USSR), D. Lozovsky (USSR), B. Grbeša (Yugoslavia), S. Semyonov (USSR), G. Kolyaskina (USSR), K. Seidel (East Germany), T. Asuni (Nigeria), L. Erlenmeyer-Kimling (USA), E. Inouye (Japan), V. Gindilis (USSR), J. Nielsen (Denmark), A. Falek (USA), D. Leigh (Britain), J. Angst (Switzerland), G. Winokur (USA), I. Shakhmatova (USSR), T. Imura (Japan), F. Kontridze (USSR), M. Mestiashevili (USSR) and S. Zulidze (USSR).

ignored all appeals about the abuse of psychiatry is probably true, but I can hardly agree with other statements by Nadzharov. I do not want foreign psychiatrists to boycott this meeting. But I hope very much that between official meetings and dinners, receptions and parties, excursions and ceremonies, some Western scientists will ask their Soviet colleagues a few specific questions. These might be some of them:

(1) Which articles of the acting legal codes in the USSR make psychiatrists punishable for unjustified placing of patients in a mental hospital?

(My reply: There is no such article in the acting legal code, because it was eliminated in 1961. In the acting legal code there is an article No. 126 which makes "illegal deprivation of freedom" punishable. An addendum to this article indicates that illegal deprivation of freedom can be considered as a crime only when a private person made this deprivation. In another article of the code (No. 178) which considers the illegal deprivation of freedom or arrest made by officials, psychiatrists are not mentioned at all.)

(2) Did the defence lawyers have the opportunity to nominate psychiatrists to observe and diagnose in any known political case?

(My reply: No. In practice the psychiatric team for political cases is selected by the prosecution and the administrators of psychiatric institutions. In most cases the nomination of such teams is the responsibility of G. Morosov, Director of Serbsy Institute of Forensic Psychiatry. Psychiatrists recommended by lawyers or relatives have never been incorporated into such teams.)

(3) Why is it that for non-political crimes the psychiatric clinics local to the courts decide on the mental health of the accused but in most political cases the decisions about mental health are always given by the same team of Moscow psychiatrists? Why was A. Snezhnevsky from Moscow the psychiatrist who advised on the case of Leonid Plyshch in Kiev?

(My reply. Because most accused persons are investigated for something they wrote or published in "samizdat". The prosecution cannot allow any local psychiatrist to read such publications and therefore only a few specially trusted and high ranking psychiatrists "trained" to study manuscripts can solve the problems of dissidents.)

(4) Why are political dissidents like Leonid Plyshch sent, after psychiatric investigation, not to the general psychiatric clinics, like most common insane criminals, but to the prison-like hospitals which according to Article 59 of the Legal Code can be used only for persons who have committed "crimes of specially grave danger" and where they are usually deprived of any rights and possi-

bility of communications with relatives and lawyers? And why are they kept there longer than allowed by the articles of the code under which they had been tried?

(My reply: I cannot explain this cruelty for people whose only "crime" is writing or distributing some kind of information.)

I would like foreign participants of this symposium to compare my replies with those they will receive from their Soviet colleagues. I would also like the British experts who will be attending this symposium to invite this special team of Soviet experts of political psychiatry to London. They could bring them to Hyde Park during the weekend to observe people speaking at spontaneous meetings. Then it will be possible to see whether the attitude of the psychiatrists to dissidents is really the same in Britain as it is in the USSR. It will be interesting to know whether Professor G. Morosov, Director of the Serbsy Institute of Forensic Psychiatry, and Professor A. Snezhnevsky, Director of the Institute of General Psychiatry, see any of the speakers and the audience as possible patients if Hyde Park were not in London, but in Moscow.

I do not advise British colleagues, however, to ask this team about my own mental state. They probably have already forgotten about my case. Recently a medical friend of mine in Britain described my own situation quite clearly. "You came to Britain after you published a book which criticized the restrictions of travel for Soviet scientists. You published in Britain a new book about Solzhenitsyn. The Supreme Soviet Praesidium deprived you of your citizenship and the Soviet Embassy here confiscated your passport. And you still hope and want to return to the USSR and you also think this will be possible? You are really mad!"

Yours sincerely,

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BRITISH ASSOCIATION

Sir Kingsley's Appeal

THE British Association for the Advancement of Science returned to the cathedrals this week. After the relative informality of last year's Leicester meeting, this year's got under way with a grand procession into Canterbury Cathedral for the conferring of degrees, the singing of a token hymn (appropriately enough "Who would true valour see, let him come hither"), and the hearing of the Presidential Address.

The last part of the operation was most worthwhile. Sir Kingsley Dunham's speech was a stern warning by a

moderate man that more attention must be paid to environmental science. "The question," Sir Kingsley said, "is quite simply, can our species survive for the next few hundred years? This dilemma is being presented at a moment when for the first time ever the techniques of systems analysis make it possible to begin to attempt to handle the considerable number of variables in the environmental picture even though verification is admittedly difficult".

"When a full assessment, based on adequate input becomes possible, it may show that economic growth has to be limited or that a more equitable distribution of its benefits must be made".



Sir Kingsley Dunham

Discussing *The Limits to Growth* and the work of Professor Forrester's group at MIT, Sir Kingsley said that it gives "in a concise form, an alarming picture which if it is correct calls for very prompt action". Sir Kingsley's criticism of the work is that the input data are inadequate. "My plea," he said, "is for the advancement of environmental science to the point where we have convincing data to work with, a reliable input for penetrative systems analysis such as could be attempted by the International Institute of Applied Systems Analysis near Vienna."

"Great moral issues almost certainly lie ahead and if it falls to environmental scientists to point the way to them, we cannot shirk the issues and say that they are none of our business . . . for more than one thousand years, the predicament of man has been thought about, talked about and prayed about in this place, the mother church of English Christendom. Like those who came before us, I believe that most of us accept the paramount values embodied in the Pauline virtues of faith, hope and charity; of which the greatest is charity in its broadest sense. But we cannot but recall that neither the Christian religion nor Science offers the expectation that man will flourish in perpetuity upon the Earth. To early Christians the

apocalypse seemed close. To those of us having some acquaintance with palaeontology, the fact that a greater number of species have become extinct than have survived is warning enough, some of these, like the ammonites, having vanished abruptly from the record after a great population explosion. Prudence demands that no effort be spared to advance those sciences which should be able to show whether the threat is real or imagined, close or distant."

"The position in the physical environmental sciences," Sir Kingsley said, "is that there is a pressing need for more widespread and exact surveys. These include surveys of mineral and hydrocarbon wealth, work on alternative energy sources such as solar energy and an assessment by meteorologists and oceanographers of the risk of the temperature of the atmosphere and seas being raised to an extent dangerous to life by increased waste heat from the energy used to produce a high standard of living throughout the world."

Sampling and surveys are equally important in the life sciences, Sir Kingsley said. So far most biologists can give only a hindsight interpretation of changes, not a prediction. Yet prediction is of the utmost importance within the framework of human ecology.

The widely separated positions held about the dangers of pollution, Sir Kingsley said, is "a measure of the inadequacy of the data so far at the disposal of scientists and economists."

A large scale chemical monitoring programme is needed, and a governmental programme of monitoring for substances other than radio isotopes is likely to be set up in the wake of last year's Stockholm conference.

"The data collecting here advocated is of the nature of survey work, but I see as the urgent task of environmental science to secure the complex information needed to test old hypotheses and to establish new ones."

Turning to the financing of this work Sir Kingsley questioned whether the resources available at present are sufficient. "I am myself too deeply involved to attempt to answer that question: it must suffice to say that . . . the cost of the effort does not amount to much more than one 0.1% of our national income."

With Sir Kingsley's speech as a keynote the conference is under way with a number of contributions running along similar lines.

A symposium on reserves, utilization and recycling of mineral wealth is part of the programme, and Sir George Porter, Director of the Royal Institution, opened the Chemistry Section meetings by declaring that "the lights will not go out in the 21st century" because chemical systems for utilizing and

storing solar energy will be developed.

Fifteen hundred people had materialized in Canterbury, at the University of Kent, by the start of the meeting, which is the first to be ruled by the association's slimmed-down committee structure. The first elected members of the general committee and council will be voted in during the course of the meeting.

FUSION

Design Team at Culham

A EUROPEAN team is to start work this month on the design of a large fusion experiment at the UK Atomic Energy Authority's Culham Laboratory. The study—which is to be carried out under the auspices of Euratom—is to be led by Dr Paul Rebut, a French engineering physicist. A team of about 20 physicists and engineers will be involved in the design of a tokamak system which is intended "to provide plasma conditions more advanced than would be obtainable in the American and Russian devices presently under construction", according to Dr R. S. Pease, Director of Culham.

The design work will take between eighteen months and two years, after which it is hoped to move immediately into construction of the experiment. The design study now proposed means that British plans announced last May to build a similar large experiment have been merged into the Euratom effort (*Nature*, 243, 51; 1973). At present, and probably for the first six months of the study, the work is being carried out under existing contracts of association with Euratom, but further funds and detailed approval from Euratom will be needed after that period. The design team is due to report on its progress to a European committee on fusion after six months.

EEC

Chairman for CERD?

LORD KENNET, the opposition spokesman on Foreign Affairs and Science Policy and one of the three British representatives on CERD, has been appointed as an adviser to the European Commission for one year. Lord Kennet succeeds Professors Aigrain of France and Casimir of the Netherlands.

Lord Kennet's appointment is very much a part-time job—a spokesman for the commission said last week that it involves about two days work a month. As adviser it is likely that Lord Kennet will take over as chairman of CERD, the advisory body which was set up last April to aid the commission on research and development matters.

But Lord Kennet's appointment does not mean that a full-time adviser to the

commission will not be appointed. The intention is still, according to a spokesman, to appoint a scientific adviser to the President of the Commission, but as yet there are no signs that such an appointment is imminent.

At a recent meeting it was suggested that CERD should be divided into sub-groups to concentrate on different aspects of research and development. This recommendation will be discussed again at the next meeting of CERD on September 17. If the fission of CERD goes ahead, then Lord Kennet will probably be responsible for the coordination of the work of the different groups.

OPEN UNIVERSITY

Links and Links

AN enthusiastic student at the Open University is attempting to forge links between the university and both the Royal Institution and the British Association for the Advancement of Science. In the August issue of *Sesame*, the university's newspaper, Mr Tony Raymond points out the advantages of such an arrangement.

The Open University, he says, is the only university without a library and the students cannot make use of any other university library. An association between the university and the Royal Institution would, for one thing, provide library facilities and it would also give students the opportunity to attend outside lectures. The events of the BA could also be attended if there was an association with it.

Mr Raymond has already approached both the bodies concerned and the response has been encouraging. A spokesman for the BA said this week that the association was interested in cooperating with any person or body that was involved in science and technology and that included the Open University.

But at this stage the possibility of links is strictly at the preliminary stage. The Open University said this week that it was giving Mr Raymond every encouragement but that it was taking no official action to help him. The next step is to see what sort of response Mr Raymond gets following his open letter to the students asking them whether they are interested in a close association with these bodies.

Perhaps the most important aspect of Mr Raymond's letter is his highlighting of the anomalous position of Open University students when they apply for membership of professional institutions. Most professional bodies have a class of membership for students but such membership usually has a basic educational requirement and an age limit, both of which most Open University students fail to satisfy.

NEW WORLD

NASA-Style Plan For Cancer Research

by our Washington Correspondent

PART of the much delayed and highly controversial National Cancer Program plan has at last seen the light of day. A blueprint for cancer research in the United States for the next five years, the plan was ceremonially handed over to President Nixon last week along with two other reports on progress in the much publicized crusade against cancer. It is a remarkable document in many respects, not least of which is that it represents a unique approach to the planning of scientific research, and it is sure to add fresh impetus to the growing debate about whether centrally directed, NASA-style management of cancer research is either timely or productive.

The fruit of some forty planning sessions involving 250 scientists which took place between October 1971 and March 1972, the plan was ultimately put together by officials of the National Cancer Institute (NCI). For some six months it has been bogged down in reviews chiefly by the Office of Management and Budget. The portion released last week, called the Strategic Plan, is a systems analysis approach to the management and organization of cancer research, setting out objectives, major courses of action and estimates of the resources that will be required for the cancer crusade in the next five years. The second part of the plan, the so-called Operating Plan, will be rather more interesting, for it will set out specific programmes to be funded and alternative ways of allocating the resources. But the operating plan will not be ready for another year and even then it will be distributed only to those responsible for managing the Cancer Program!

The strategic plan describes itself as a disease-orientated approach to the administration of cancer research. To achieve the ultimate goal of developing "the means to reduce the incidence, morbidity and mortality of cancer in humans". The plan sets out seven major objectives ranging from prevention to rehabilitation. The objectives are then defined in terms of "approaches"—for example, "reduce development of cancer by altering immunological capability of individuals" — and these are further broken down into "approach elements" and "project areas", which is where actual research projects fit into the picture. The plan, simplified into a diagram with the goal at the centre and the objectives radiating from it like spokes of a wheel, has been hanging on some

laboratory walls at the NIH campus in Bethesda for several months where it has been treated with various degrees of respect and has even been found to make a good dart board.

While it is no small feat to assess the staggering amount of research bearing on cancer and to set out an overall set of goals and strategies, the tricky and more controversial questions of how much money should be devoted to individual projects or different approaches, is not spelled out in the strategic plan unveiled last week—those questions will be tackled in the operating plan, which is one reason why it is not yet ready. But the Strategic Plan does give estimates of the total resources that will be required for the cancer crusade in the next five years.

By 1978, the plan would require some \$1,200 million to be spent on cancer research in the United States, of which about \$850 million would be provided by the National Cancer Institute. (The rest would come from other Institutes of the National Institutes of Health, State and Local Governments and volunteer organizations.) That total compares with about \$512 million spent in 1971. As for the NCI itself, the plan suggests that its budget for the 1974 fiscal year (which started on July 1) should be \$500 million, in other words, the same amount as the Administration

has already requested, and that it should increase steadily over the next five years by an average of about \$65 million a year. By 1982, the plan envisages that the total cancer crusade will be consuming some \$1,700 million a year.

As far as manpower is concerned, the plan warns that "the unavailability of required scientific manpower may constrain achievement of the program target operating level". Some 9,300 scientists will be required in 1978 for the portion of the cancer programme operated by the NCI alone, while only about 5,000 scientists are now involved in NCI-supported cancer research. Can present training programmes meet the demand? Those who drew up the plan believe not, for they suggest that a "deficiency in the number of scientists continue to increase as the program expands". It should be pointed out, however, that the plan was drawn up before the recent announcement that at least part of the NIH training programme is to be saved from the budgetary axe (see *Nature*, 244, 128; 1973).

The plan is sure to generate some criticism about its specific conclusions and recommendations, but it has already sparked considerable controversy over the more fundamental issue of whether or not cancer research is amenable to the systems analysis approach that the plan takes. In particular, is the move towards tighter central planning likely to stifle creativity? And is the increasing emphasis on cancer likely to take funds away from equally deserving areas of biomedical research?

Those questions have been raised increasingly in the past few years particularly in regard to the growing use of contracts as opposed to grants to fund biomedical research. Many of these were set out in a review of the strategic cancer plan carried out last year by the Institute of Medicine, part of the National Academy of Sciences. The institute's review, which has not been made public but which has been extensively leaked, raised objections to some specific points in the plan but criticized it chiefly for leaving the impression that all shots can be called from a central headquarters, that all, or nearly all, of the really important ideas are already at hand, and that given the right kind of administration and organization the hard problems can be solved.

The institute suggested that a centrally planned, accelerated research programme may be applicable to a small number of cancers for which therapeutic technology is relatively effective and

Cancer Panel

PRESIDENT NIXON announced last week that he has appointed Dr Ray D. Owen, Professor of Biology at California Institute of Technology, to be a member of the President's Cancer Panel. A three-member board charged with monitoring the development and execution of the National Cancer Plan, the panel report directly to the President on any blockages or delays in carrying out the programme. It is thus an influential body. It was also announced that Mr Benno C. Schmidt, managing partner of J. H. Whitney and Co, has been re-appointed chairman of the panel for a second term of one year. Dr Owen replaced Dr Robert A. Good, whose term of office expired on February 22. The third member of the panel is Dr R. Lee Clark, director of the M. D. Anderson Hospital and Tumor Institute in Houston.

where the direction that research should take is reasonably clear. Included in that group are acute childhood lymphatic leukaemia, Hodgkins disease, choriocarcinoma, Wills' tumour, carcinoma of the cervix and some skin carcinomas. But for the majority of cancers a NASA style assault may not be the best approach since the way ahead for research is "not at all clear". The institute suggests that research on such cancers "ought to involve rather less in the way of centralization, and rather more of a tendency towards decentralization". The institute puts into a nutshell many of the arguments against strong central planning of basic research.

"What is most urgently needed for problems of this kind is an abundance of new ideas and these are most likely to emerge from the imagination of individual scientists . . . it is much less likely that the administrators of large programs, or committees of administrators, at the centre of a highly centralized bureaucracy, can generate the kinds of ideas that are needed".

In particular, the trend towards central control and planning of cancer research has generated two highly controversial issues in the funding of research in the USA. The first is a move towards more contract research as opposed to grants (more than 50% of the research supported by the NCI is now accounted for by contracts), and the second is an attack on the peer review system by which NIH grants are funded. The two issues are closely intertwined, and they represent considerable change in the operation of biomedical research.

The traditional way of determining which research should be funded by NIH is by committees of scientists which examine grant proposals submitted by individual researchers and rate them according to their scientific merit. The final funding decision rests with NIH officials, but the peer review mechanism is perhaps the most influential part of the process, and it is jealously guarded. A recent memorandum prepared by the Office of Management and Budget suggested, however, that the peer review system "is not readily compatible with targeted research or directed research to achieve specific national objectives", and suggested several ways of "improving" the system, including abolishing it (see *Nature*, **243**, 256; 1973).

The cancer plan specifically stated, however, that the peer review system will continue to be utilized for review of research proposals submitted by those individuals who wish to apply for support through the grant mechanism. But it had little to say about the trend towards contract research, except to point out that "the assessment of contract proposals for scientific merit is as important as grant proposals". One concern is that if contract research con-

tinues to grow, it will take money away from investigator-originated research. Dr James Watson of Harvard University, recently told a Congressional Committee, for example, that "the forthcoming governmental prescription for cancer research . . . ominously points in the direction of more contract money, in which the individual scientist decides where the future may lie".

Another central question about the crusade against cancer is that it may be swallowing up funds for other areas of biomedical research. Such charges, in fact, seem to have some substance since every Institute in NIH except for the National Cancer Institute and the National Heart and Lung Institute suffered budget cuts last year. The Institute of Medicine said in its review of the plan, for example, that many areas of basic biology may be crucial to the cancer programme, and pointed out that "it would be a dead loss to the cancer effort if research of this kind were to go without support because of fund shortages in other institutes of NIH".

SKYLAB

Preparing for Kohoutek

by our Washington Correspondent

NASA officials are studying plans to delay launch of the third and final Skylab crew for 10 days in order to get a better look at the comet Kohoutek. Predicted to be one of the most interesting and perhaps the most spectacular comets this century, Kohoutek will swing behind the Sun, reaching perihelion (its closest approach to the Sun) on December 28, and will pass closest to the Earth on January 15. Skylab is now set for launch on November 9 and splashdown in the Pacific on January 4, and so a 10-day delay will enable closer study of the comet after its perihelion has passed.

The original launch schedule would allow the comet to be studied during its approach to the Sun and for a short time after perihelion. But it would miss the period during which the comet will be cooling down, when it so happens that the Earth will be in the best position to view the tail. A new ultraviolet camera will probably be added to Skylab's instruments in any case, and the Apollo Telescope Mount will be used to view the comet over a wide spectral range at perihelion.

In addition to Skylab, NASA is hoping to look at Kohoutek with instruments aboard several other spacecraft. The Orbiting Solar Observatory (OSO-7) will be used to view the comet at perihelion, while OAO-C (Copernicus) will turn its instruments towards Kohoutek as the comet approaches and recedes

But the actual level of support recommended for cancer research in the plan is likely to become a controversial issue in itself, aside from the question of whether it is soaking up money from other research.

It is suggested in the plan that the NCI should receive \$500 million next year, which is the same amount as the administration requested. But the National Cancer Advisory Board, whose annual report was published last week, recommended that \$600 million should be made available. Moreover, the plan calls for a budget for the NCI in 1975 of about \$600 million but a preliminary budget plan drawn up by Dr Charles C. Edwards, the Government's top health official, which was recently leaked to Senator Edward Kennedy, recommends an increase in the NCI's budget of only \$25 million. That would fall some \$75 million short of the level proposed in the plan. It is thus likely that the most prominent debate about the cancer programme is how much money it should receive. But it is clear that more basic issues are involved.

from the Sun. (Copernicus cannot turn its instruments and its solar panels towards the Sun at the same time.) The Mariner Venus-Mercury spacecraft, which is set for launch on November 3, and the Pioneer spacecraft which are on their way to Jupiter will also be used to study Kohoutek, and in addition NASA is planning to launch sounding rockets and to use high-altitude aircraft. There has also been talk of sending an Explorer spacecraft directly into the tail of the comet, but it seems that idea has been shelved because of lack of money, although there is a proposal under consideration to send an Explorer to the Grigg-Skjellerup comet in 1977.

One reason for the intense interest in comets is that if they were formed outside the orbit of Neptune, as one widely-held theory suggests, they may consist essentially of primordial solar system material largely unmodified by solar radiation. That would be especially true of a long period comet such as Kohoutek, which is reckoned to have an orbital period of several thousand years.

A decision on the final Skylab launch date will not be taken until after the present mission is completed, but there is a possibility that the launch, instead of being put back, may have to be brought forward to reduce the length of time that the laboratory will be unmanned; the decision hinges chiefly on an assessment of the condition of the spacecraft at the end of the present mission. But if the launch is brought forward, the chance of using Skylab's instruments to observe the comet may be missed entirely.

NEWS AND VIEWS

Measuring the Speed of Light More Accurately

WITH the increasing interest in space communications and in the correlation of optical astronomical data with those obtained by radio astronomy, much effort has recently been devoted to a more accurate measurement of c , the velocity of light, which relates wavelength to frequency. Although the present length standard, the krypton-86 605.7 nm visible wavelength standard, has a reproducibility of one part in 10^8 , and the present frequency standard, the caesium atomic beam, has a reproducibility of one part in 10^{12} , the value of c previously accepted had an accuracy of one part in 10^6 .

The reason for this low accuracy compared with that of the length standard, which in principle limits the determination at present to one part in 10^8 , is associated with the wavelength of the radiation at which the comparison of frequency and wavelength was carried out. In order to achieve high precision wavelength measurements it is necessary to work at wavelengths of 10 μm or shorter. But at the time when Froome measured c at the National Physical Laboratory (*Proc. R. Soc.*, **247**, 109; 1958) it was not possible to measure the frequency of sources in the optimum region, and the measurements were made in the microwave region. In this region the wavelength of the sources is comparable to the dimensions of the interferometer used for the wavelength measurements so that large diffraction corrections are necessary.

Since the earlier experiments were carried out some highly stable laser sources have been developed in the region from 10 μm to 700 nm, and the frequencies of some of these have been measured. The most promising of these sources are the CO_2 lasers oscillating between 9 μm and 11 μm stabilized on a very narrow fluorescence signal from an intracavity passive CO_2 cell, the 3.39 μm helium-neon laser stabilized at the centre of the saturated absorption line of methane, and the 632.8 nm helium-neon laser stabilized on one of the molecular iodine saturated absorption lines which lie under the doppler gain profile. The wavelengths of all of these sources have been measured

relative to the length standard and a reproducibility of one part in 10^9 can be obtained once corrections are made for the asymmetry of the krypton emission line (*J. Phys. E.*, **6**, 647; 1973; *Appl. Phys. Lett.*, **22**, 196; 1973; and *Opt. Commun.*, **6**, 91; 1972). A comparison of the wavelengths of these sources measured in different laboratories shows a reproducibility of the order of one part in 10^9 .

In order to measure the frequencies of the sources it is necessary to construct a chain of harmonic coincidences between sources which are suitable for transferring measurements from the caesium standard to the appropriate comparison line. In order to achieve this a set of efficient harmonic mixing devices have had to be developed, principally by Evenson and his collaborators. So far lines of the CO_2 laser and the 3.39 μm saturated methane line have been measured in this way. The frequency of the 3.39 μm line was measured by Evenson and his colleagues in three stages (*Appl. Phys. Lett.*, **22**, 192; 1973). In the first stage the frequency of the R10 line of a stabilized 9.3 μm CO_2 laser was measured relative to that of the caesium standard using a harmonic chain involving two klystrons, a 337 μm HCN laser and a 28 μm H_2O laser. In the second stage the frequency of the R30 line of a 10.2 μm CO_2 laser was measured relative to the 9.3 μm line, and in the third stage the frequency of the methane line was measured relative to that of the 10.2 μm line. On page 504 of this edition of *Nature*, Blaney *et al.* report the absolute frequency measurement of the R(12) transition of CO_2 at 9.3 μm . Used in conjunction with the R(12)—R(10) difference frequency recently determined at the National Bureau of Standards, the agreement with the frequency of the R(10) line used in the velocity of light experiment is within three parts in 10^{10} . This reproducibility is a good test of the accuracy of this method of frequency measurement.

It is possible that in the future either the 3.39 μm saturated methane line or one of the 632.8 nm saturated iodine lines may become the new

length standard, since both lines are sharper and probably more symmetrical than krypton 86, and seem to have a reproducibility of the order of one part in 10^9 . This would allow the velocity of light to be defined to an accuracy of one part in 10^9 , which is the limit set by the present determination of the alternative length standards.

From a Correspondent

MUSCULAR DYSTROPHY

Blood Cell Abnormality?

from a Correspondent

MYOTONIC muscular dystrophy (dystrophia myotonica) is a disorder of autosomal dominant inheritance, characterized clinically by progressive weakness of distal limb, facial and neck muscles, which usually first becomes manifest in adolescence or early adult life and is slowly progressive, leading as a rule to severe disability in middle life and to death well before the normal age. The phenomenon of myotonia is seen most readily in the tongue and in forearm muscles and is usually easily recognized both clinically and electromyographically.

It has been well known for many years that the disease is not one which is limited to the voluntary musculature, for constant abnormalities in affected patients include frontal baldness (in the male), testicular atrophy, cardiomyopathy, malformation of cranial bones, disturbances of smooth muscle motility, cataracts and extrathyroid hypometabolism. Although many patients demonstrate abnormal glucose tolerance with enhanced serum insulin levels and hypercatabolism of immunoglobulin, no constant or specific generalized metabolic defect has yet been demonstrated. A muscle membrane defect has been postulated to account for the myotonia and perhaps also for the progressive muscular weakness (Denny-Brown and Nevin, *Brain*, **64**, 1; 1941; and Landau, *Neurology, Minneap.*, **2**, 369; 1952), but McComas and Mrozek found (*J. Neurol. Neurosurg. Psychiat.*, **34**, 441; 1968) that although the resting membrane potential of many muscle fibres was reduced in patients suffering from the disease, the impedance of the muscle fibre membrane appeared to be normal. McComas, Campbell and Sica suggested (*J. Neurol. Neurosurg. Psychiat.*, **34**, 132; 1971) that as the disease progresses, there is an increasing loss of motor units in the extensor digitorum

brevis muscle of the foot and they postulated a primary defect of motor innervation. Histochemical studies of muscle biopsies from such patients have shown a consistent atrophy of type I (slow-twitch, oxidative enzyme-rich) muscle fibres (Engel, *Proc. Int. Congr. Neurol., Vienna*, 2, 67; 1965).

Now for the first time a study by Roses and Appel (*Proc. natn. Acad. Sci., U.S.A.*, 70, 1855; 1973) has suggested that in such patients there may be a consistent and reproducible metabolic abnormality demonstrated in erythrocyte membranes or "ghosts". They prepared the erythrocyte ghosts from blood samples obtained from fasting patients with myotonic muscular dystrophy and compared their findings in these individuals with those obtained on similar samples derived from control subjects matched for age and sex. When the ghosts were incubated with [γ - 32 P] ATP, there was no significant difference in the degree of labelling of ghost proteins if fresh preparations were used. But when the experiments were carried out after storing the ghosts at -20° C for 7 days the incorporation of 32 P in the controls was twice as high as in fresh preparations, whereas that in the myotonic ghosts was unchanged and was now significantly less than the controls. On the other hand, freezing in dry ice and thawing immediately increased phosphorylation in both groups, with no significant difference between them. No differences could be demonstrated in phospholipids, gangliosides or sialoproteins or in the membrane polypeptide electrophoretic profiles with control and myotonic ghost preparations.

The diminution in endogenous erythrocyte protein kinase was not likely to be attributable to differences in substrate, because the K_m for ATP was identical and the polypeptides to be phosphorylated were electrophoretically identical in normal and myotonic preparations. The ability of acute frozen erythrocyte polypeptides from myotonic patients to be phosphorylated at twice the rate for fresh or aged frozen preparations also suggests that the amounts of protein substrate were not responsible for the differences noted in enzyme activity. As the authors comment, it is unclear whether the lower than normal protein kinase activity which they found in 7-day frozen myotonic preparations was the result of an intrinsic change in enzyme protein or of a change in the state of the membrane associated with a less stable configuration of the enzyme protein, or to an altered reactivity with its specific substrates.

These results are difficult to interpret, but suggest that there may be a specific structural or metabolic abnormality in the circulating red blood cells in patients with myotonic dystrophy which, if it can be confirmed, demands further in-

vestigation. Clearly more work is now required on membrane-bound protein kinase in muscle tissue and further studies are needed to characterize and extend these observations relating to the involvement of the erythrocyte membrane in this disease process.

MEMBRANES

Phases for Ases

from our Molecular Biology Correspondent
SINCE Danielli brought the tablets down from the mountain, the membrane field has come close to being engulfed by such a rapidly swelling flood of information about the phospholipid bilayer that biochemists might do well to head for the hills. There is scarcely a physical technique that has not been pressed into service, be it X-ray diffraction, Raman spectroscopy, calorimetry, ESR, proton, deuteron, carbon, nitrogen or phosphorous NMR — but enough; for the question remains whether the welter of facts, phenomena and conjecture leads to any coherent picture of how membranes actually perform their physiological tasks, in particular selective transport of solutes. For all that is known about the behaviour of lipids and phospholipids in membranes and models, there is an enduring dearth of hard information about how this relates to the structure and activity of the proteins embedded in them, which among other things are the agents of transport.

The most interesting evidence of a direct relation between enzymatic activity and the physical nature of the bilayer comes from comparisons of the effects of temperature on both. It is well established that real and artificial membranes undergo a profound change in character at a critical temperature, the value of which depends on the lipid composition. Above this temperature the membrane is essentially disordered, with rapid rotational and translational diffusion of lipid molecules in the plane of the bilayer, and uninhibited mobility of the hydrocarbon chains towards the centre. Below the critical temperature the structure is essentially frozen into a hexagonal lattice, the hydrocarbon chains being tightly packed in the all-*trans* configuration. The critical temperature may therefore properly be regarded as marking an order-disorder phase transition.

In membranes that contain lipids with *cis* ethylenic bonds, the ordered state is destabilized, the transition temperature is lowered and the discovery of bacterial auxotrophs for unsaturated fatty acids has therefore made it possible to vary the critical temperature of *Escherichia coli* membranes almost at will. Overath and Träuble (*Biochemistry*, 12, 2625; 1973) describe the properties of cells grown in the presence of different *cis* and *trans* monounsaturated fatty acids. They show that the thermal phase transition can be observed by a variety of simple methods, such as dilatometry, turbidimetry and fluorescence of mem-

mRNA in Health and Disease

Two communications in *Nature New Biology* next Wednesday (August 29) resolve outstanding questions concerning the life history of mRNA in eukaryotic cells. Bryan and Hayashi have posed the question: are proteins bound to mRNAs in eukaryotic cells in general, and, if so, are they the same proteins which are known to be bound to globin mRNA in the same organism? Two proteins—so far characterized only in terms of molecular weight, one, 49,000–52,000, and the other, 73,000–78,000, estimated by polyacrylamide gel electrophoresis in SDS—are known to be associated with globin mRNA. These messenger ribonucleoprotein (RNP) particles are released on the dissociation of reticulocyte polysomes into subunits.

Bryan and Hayashi performed similar experiments on pulse-labelled chick embryo cerebral polysomes (salt-washed to remove contaminating proteins) and isolated messenger-containing particles sedimenting in the range of 10–30 S, 50 S and 70–200 S. All three fractions contained two proteins of molecular weights 48,400 and 78,500, estimated by SDS gel electrophoresis. These authors

also found that reticulocyte globin mRNA yields proteins of 47,000 and 77,000 in agreement with the earlier work. Bryan and Hayashi cite contemporary published works by Blobel claiming that mRNA of L cells and rat liver polysomes likewise bind proteins of 52,000 and 78,000 molecular weight. The results, taken together, indicate that a wide variety of messengers are associated with two proteins with the same molecular weight distribution. Whether the proteins are identical in different messenger particles can be settled only by more rigorous comparisons.

Hatta *et al.* have traced the deficiency of the β chain of haemoglobin in β -thalassaemia patients back to its origin in the erythroblasts of bone marrow. The question they have resolved is whether the known deficiency in circulating reticulocytes is caused by selective nucleolytic destruction of the β -globin mRNA at an earlier stage, or by reduced synthesis of this mRNA. De-ranged control at the level of DNA transcription seems to be the primary cause of β thalassaemia in the case studied by these authors.

brane-soluble dyes. The transition occurs between 40° C for a typical all-*trans* species and 14° C for one containing a *cis*-ethylenic bond. The transition temperature is largely determined by the preponderant membrane lipid, phosphatidylethanolamine. A striking feature emerges once more from the temperature dependence of transport-linked functions, such as hydrolysis of a galactose ester by the cells: when expressed in terms of Arrhenius plots, the hydrolytic rates show two linear phases in all cases, with a sharp discontinuity precisely at the critical temperature, determined by the unsaturated fatty acid made available during cell growth. Thus the activity of the corresponding transport enzyme is inhibited when the lipid phase solidifies.

The demonstration of how the composition of the bilayer relates to the membrane assembly process represents a noteworthy advance in linking its physical properties to function. Tsukagoshi and Fox (*ibid.*, 2816), following their earlier observation that different transport processes, based on unrelated enzyme systems, evince a change of activity at the same critical temperature, have now shown that induction of the lactose transport system in *E. coli*, measured by levels of enzymatic activity, fails below a critical temperature, which is again identical to that of the lipid phase transition, and depends accordingly on the nature of the fatty acid supplement. Tsukagoshi and Fox (*ibid.*, 2822) go on to show that the transition temperature for transport activity can be progressively varied by switching from one fatty acid to another during growth, if the temperature is above critical. If the transport system is induced at a temperature below the critical after switching from one fatty acid to the other, a new phenomenon supervenes: the Arrhenius plot shows three phases. The second discontinuity can be eliminated by, as it were, annealing the cells above the transition temperature. The inference is that below the bilayer melting temperature, the transport enzymes are insinuated into the membrane in their own pool of freshly synthesized lipid. If this is of a type associated with a high melting temperature, then these ice-floes will survive after the rest of the membrane, with its own population of enzymes has melted, to melt ultimately at their own characteristic temperature. When the growth temperature is above critical the new lipids which result from the fatty acid switch will simply be dispersed in the fluid membrane, along with the induced enzyme, and the critical temperature will simply reflect the average composition.

The dependence of the activity of a transport enzyme on the fluidity of the bilayer has also now been demonstrated

in an animal system: Grisham and Barnett (*ibid.*, 2635) find that at 20° C the activation energy of the sodium-potassium ATPase of outer kidney membrane undergoes a twofold change, and at the very same temperature the signal from a spin label in the membrane manifests a convulsion. These experiments were done on a complex of the enzyme with its characteristic complement of lipids. When these are extracted from the preparation and examined as a protein-free bilayer, they show the same phase change, from which it follows that it is the lipid that controls the state of the enzyme, not the converse. Grisham and Barnett also show that the lipid environment of the enzyme is appreciably different from

that of the membrane as a whole, for spin labels on long fatty acid esters, that project deep into the bilayer record greater fluidity in the purified ATPase membrane, whereas a label closer to the head groups, no mobility difference is in evidence. Similar breaks in the Arrhenius plots for two enzymes in microsomal membranes have been observed by Eletr, Zakim and Vessey (*J. Molec. Biol.*, **78**, 351; 1973). Comparison with phase transitions in the bilayer, recorded by spin labels, before and after sonication and following phospholipase treatment, indicates that the two enzymes are surrounded by atmospheres of phospholipid differing appreciably in composition.

One of the most rewarding areas—

Forever Blowing Bubbles

Two novel communications, one theoretical and one experimental, on the mechanism of DNA replication appear in *Nature New Biology* next Wednesday (August 29). The theoretical paper by Ioannou proposes a general model to account for all the known facts about DNA replication; Hobom and Hobom present experimental evidence for a model for λ dv replication, which appears to be an exception to the rule that RNA is necessarily involved in DNA replication.

Ioannou's model of DNA replication contains the following essential points. DNA replication is based on units of replication which he calls "unitrons", of which there are many, separated by variable distances in different DNA species. After two breaks in the DNA at opposite ends of the unitron, an RNA complement of the two free 3' ends, consisting of about fifty ribonucleotides, is made. This RNA-DNA hybrid serves as a primer for the synthesis of DNA complementary to the remaining single strands of DNA in the unitron. The resultant four stranded structure is called a "microbubble". The RNA is then excised, and according to the model, the microbubbles condense to form "macro-bubbles". The single stranded DNA corresponding to the previously stable double stranded regions of about 100–200 nucleotides long is then copied by the normal repair mechanism and the nascent DNA segments are joined by DNA ligase.

The model is consistent with many known features of DNA synthesis. Unidirectional replication would require an impossible rate of unwinding DNA, about 10,000 r.p.m. Multiple sites for DNA initiation have been found in replication systems of phages, prokaryotes and eukaryotes. Macro-bubbles have been observed by electron microscopy and autoradiography. The

model is consistent with the size of Okazaki fragments, known intermediates of DNA synthesis. An RNA primer is known to be universally involved in DNA synthesis in viruses, bacteria and higher organisms. Inhibitors of RNA synthesis, rifampicin and streptolydigin, inhibit only the initiation of DNA replication.

The model is elaborated to demand, generally, a two-fold rotational axis of symmetry perpendicular to the helix axis at each end of the unitron. Such regions are known to be common in DNA. DNA unwinding enzymes have been characterized in a number of systems. The RNA primer could be removed exonucleolytically either by RNase H or DNA polymerase I. The growth of macrobubbles may depend on cytoplasmic factors accounting for bidirectional and unidirectional DNA synthesis observed at the replicating forks of DNA.

Hobom and Hobom accept the idea that an RNA primer is generally required for DNA synthesis, but seem to have found an exception to the case in the replication of λ dr DNA. Their evidence is based on the resistance of replication of this mutant to inhibitors by rifampicin. They propose an alternative model for DNA replication which is possible owing to the special structure of λ dv DNA. According to their model the DNA is present as a dimer replicon with two origins of replication opposite each other on a circular DNA molecule. Bidirectional replication of λ dv starting at the end of one or other of the origins is predicted to lead to termination reactrons localized on the DNA molecule very close to the second site of origin. They suggest that the remnants of these reactions—short pieces of DNA strands—may be re-usable for priming the next round of initiation at this second site of origin.

in more senses than one—in the study of membranes just now concerns transformed cells in tissue culture, which as all the world knows show enhanced agglutinability by lectins. Noonan and Burger (*J. Biol. Chem.*, **248**, 4286; 1973), aside from showing that the phenomenon is not only (as has been suggested) the result of greater membrane fluidity, but also of a greater number of available binding sites, have demonstrated a precipitous change in the amount of concanavalin A bound at 15° C, which again is a manifestation of a bilayer phase transition.

For students of the tricks of bilayers, Michaelson, Horwitz and Klein (*Biochemistry*, **12**, 2637; 1973), have demonstrated a tendency of particular phospholipids to collect preferentially on the inside or outside surface of vesicles, according to their ionic nature, and McNamee and McConell (*ibid.*, 2951) have found that in electroplax membrane vesicles there is a continuous migration of phospholipids back and forth between the inner and outer surface on a time scale of a few minutes at 15° C.

LOCUSTS

Pheromone Identified

from a Correspondent

PHASE transformation in locusts refers to the changes induced when solitary hoppers (juvenile locusts) become gregarious. The process is reversible in the instar stages because it is dependent upon the insect's population density. Gregaria hoppers are more active, need more food and are darker in colour than the solitaria hoppers (the latter are a green to fawn colour); and the gregaria adults assume longer wings and broader heads than their solitary counterparts. There is, however, one feature of the gregaria phase that can be measured more accurately than behavioural and physiological phenomena; during meiosis in the swarming adult male, the frequency of chiasmata (genetic crossing over) is increased as much as 30% over that of solitary males (Nolte, *Chromosoma*, **21**, 123; 1967).

Chemical communication plays a dominant part in the behaviour of locusts. In the desert locust, *Schistocerca gregaria*, olfactory information is important for food seeking, for synchronizing maturation, and for localizing oviposition. It was on this basis that Nolte (*Nature*, **200**, 660; 1963) postulated the liberation of a pheromone (a substance secreted to the outside of an individual and received by a second individual of the same species, in which it releases a specific action) by massed locusts that would trigger off gregarization processes. Nolte *et al.* (*Chromosoma*, **29**, 462;

1970) later found that the postulated pheromone was excreted in the faeces of solitary and gregarious hoppers (but not of the adults). The production of the pheromone was found to be related to the crop section of the alimentary tract and perception of such a stimulus appeared to be through the spiracles directly into the haemolymph.

Nolte *et al.* (*J. Insect Physiol.*, **19**, 1547; 1973) have now obtained evidence that this pheromone is 2-methoxy-5-ethylphenol, a derivative of guaiacol, which is a degradation product of the metabolism of the lignin of plants. They postulate that lignin is ingested in grass or shrubs and degraded in the crops of the larvae to guaiacol, some of which is excreted in the faeces, and the rest changed to the active pheromone (called "locustol") and also excreted.

The pheromone and some other substances were extracted by steam distillation and pentane extraction of hopper faeces. Gas chromatography of the pentane extract and preparative thin-layer chromatography of a more intensely purified extract disclosed two major and several minor components. Mass and nuclear magnetic resonance spectroscopy suggested that the two major substances are guaiacol (O-methoxyphenol) and 2-methoxy-5-ethylphenol, and this was confirmed by comparison of the effects of the two extracts and the two synthesized suspected compounds (and some of their isomers) on gregarization.

Four characteristics of gregarization in *Locusta migratoria migratorioides* were used in the identification of the pheromone: colour change during the various instars; chiasma frequencies during the first few days after becoming adult; adult morphometric ratios; and behavioural traits. Chiasma frequencies of the eight largest autosomes (the three shortest invariably exhibit one chiasma per pair) provided the most sensitive index of gregarization. Of the other criteria involved, pigmentation is influenced by other external factors (for example, humidity) as well as by chemicals, morphometric ratios are somewhat restrained under laboratory conditions and behaviour is difficult to standardize.

Considering these four criteria, locustol was shown to be the most active constituent of hopper faeces, although several other substances were shown to possess varying degrees of activity on one or more of the gregarization traits. Thus in a congregating group of hoppers gregarization will be triggered off by the accumulation of locustol in the atmosphere around the group. Previously, gregarization was found not to be so prominent a phenomenon in well ventilated laboratories. The ecological significance therefore in field conditions of a phenomenon that seems to depend on the build-up of a substance in a confined space has yet to be assessed.

SOLID STATE PHYSICS

Energetic Phonons

from our Condensed Matter Correspondent

IN a recent issue of *Physical Review Letters* (**31**, 215; 1973) Welte and Eisenmenger of Stuttgart University report that they have succeeded in generating extremely energetic phonons, with frequencies ν in the region of 1 THz (10^{12} Hz), by using superconducting aluminium tunnel diodes.

The thermal energy of a crystalline solid takes the form of quantized lattice vibrations, known as phonons. From the thermodynamic point of view, a simple solid may be regarded as an empty box containing a large number of phonons, each of energy $h\nu$, behaving very much like a gas of rapidly moving free particles. Phonons of low frequency and energy travel at the velocity of sound. Their velocity falls with increasing frequency until, at the so-called Debye cutoff frequency ν_D , which is characteristic of the material, their velocity becomes zero. Phonons of frequency greater than ν_D are not a very meaningful concept since they would have wavelengths shorter than the interatomic spacing.

At high temperatures the mean free path λ of the phonons is very short because phonon-phonon collisions are frequent. But at temperatures near 1 K, at which relatively few thermal phonons are present, λ can become comparable with the dimensions of the specimen; this situation is analogous to the molecular flow regime of a low pressure gas. A high energy phonon introduced at one end of the specimen has, therefore, a high probability of continuing in a straight line until it strikes a boundary so that, by using a suitable phonon generator and detector, the passage of a pulse of phonons across the specimen can be investigated. Unfortunately, conventional techniques for generating phonons are either restricted to relatively low frequencies, much less than ν_D , or produce phonons which are not monochromatic but spread over a wide range of frequencies.

While working with A. H. Dayem at the Bell Telephone Laboratories, however, Eisenmenger was able to report in an earlier paper that a superconducting

Correction

As the result of editorial error, Professor J. Yvon, of the Commissariat à l'Energie Atomique (CEA) in Paris, was inadvertently described in the News and Views article "Molecular Motions" (*Nature*, **244**, 256; 1973) as coming from the University of Paris; so, too, was Dr P. Lallemand, of the École Normale Supérieure.

tin tunnel diode can be used as a generator of relatively high energy phonons (*Phys. Rev. Lett.*, **18**, 125; 1967). Such a junction consists of a sandwich of two thin layers of superconductor separated by a very thin layer of insulator, and is prepared by evaporating the materials under high vacuum. When a suitable voltage V is applied between the electrodes, electrons are able to "tunnel" through the insulator, and arrive in the positive electrode with an excess energy of eV . It was found that, if the bias voltage was chosen so that eV was greater than twice the energy gap Δ (separating the ordinary electron states from the lower energy, paired, superconducting states) of the tin, most of the injected electrons gave up their excess energy in a two stage process: they fell first to the top of the energy gap by emission of a phonon or phonons whose maximum energy must be $eV - 2\Delta$, and then dropped into a paired state with emission of another phonon whose energy was always 2Δ .

The experimental arrangement consisted of a diode formed on the end of a sapphire rod, so that the phonons which were generated could escape and propagate freely in the sapphire. A second diode was used to detect their arrival at the other end of the rod. Unfortunately, it turned out that phonons generated by the first process, known as relaxation phonons, were unable to escape from the diode, being strongly absorbed by the tin and giving rise, ultimately to further phonons of energy 2Δ , which is a great deal less than v_D for most materials.

In their latest experiments, the Stuttgart group has been able to show that, for aluminium junctions, the energy of the emitted phonons is not limited to 2Δ , probably because the electron-phonon interaction is smaller than for tin, so that the relaxation phonons have a better chance of escaping.

The phonons were allowed to propagate in a silicon crystal. In order to show convincingly that they really were dealing with phonons of energy up to $eV - 2\Delta$, they "doped" the silicon with a little oxygen, since infrared studies have shown that there is then a very strong resonant absorption of energy at 29 cm^{-1} ; and they report that they did indeed observe a phonon absorption line at an energy within 1% of the predicted value, which was at about 24Δ , corresponding to a frequency of 0.87 THz . Forkel *et al.* believe that their technique should enable phonons to be generated right up to the Debye limit of $v_D = 9.5\text{ THz}$ for aluminium. If they are right, there should follow a whole series of elegant experiments designed to investigate the behaviour of very high energy phonons in a variety of different materials.

PALAEOMAGNETISM

Misidentified Dyke

from our Geomagnetism Correspondent

It is a long time since palaeomagnetism surprised most of the geological community by giving the first convincing quantitative evidence in favour of continental drift and thus setting the scene for the new global tectonics. But it can still come up with a geological surprise, albeit a more minor one, from time to time, even in a country as much studied geologically as Britain. Much of the more obvious geology of Britain was investigated in detail during the nineteenth and early twentieth centuries, of course; but it would appear from recent work that even its well and long established tenets are not necessarily immune to the onslaught of modern techniques.

Consider, for example, the Wackerfield Dyke near Staindrop in County Durham, which was studied in detail many years ago by Holmes and Smith (*Durham Geol. Mag.*, **58**, 440; 1921). Although this roughly WNW-trending dyke is not exposed continuously, it is fairly obvious from field relations that it forms part of the Cleveland-Armathwaite Dyke. The latter, in turn, is part of the Eocene Mull Dyke Swarm which, though intense in western Scotland, thins out across southern Scotland and nor-

thern England into a much smaller number of larger dykes. Northern England, however, also contains an earlier generation of basic dykes and sills exemplified by the Upper Carboniferous Whin Sill, a system of transgressive quartz dolerite sheets which are intermittently exposed. Generally speaking, the Whin Sill and associated exposures do not follow the clear WNW trend of the Mull Dyke Swarm extension, although, being more erratic in direction, some of the exposures near the Cleveland-Armathwaite Dyke do lie roughly WNW. In spite of this superficial confusion, however, the Wackerfield Dyke has always been regarded as part of the Tertiary activity.

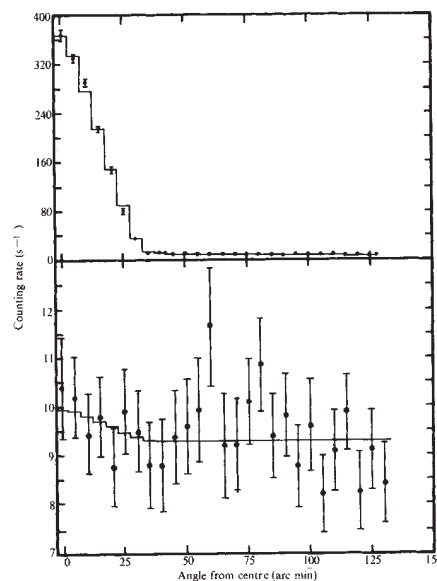
But Tarling *et al.* (*Earth planet. Sci. Lett.*, **18**, 427; 1973) have now used palaeomagnetic and isotopic dating techniques to show that this long-cherished belief must be discarded. The critical palaeomagnetic data come from fresh, unweathered samples of the Wackerfield Dyke exposed by quarrying, although comparative tests were also carried out on samples from the zone of surface weathering. Both thermal and alternating field demagnetization tests show that the natural remanent magnetizations of the fresh samples are extremely stable, and this is confirmed indirectly by the petrology. In the fresh samples, titan-

Are There Two Kinds of Radio Star?

It is not long since the discovery of a radio source associated with a star ranked as an event of major importance in astronomy. Now, however, several such associations are known, and astronomers have moved on to the next stage in studying these objects—trying to find family relationships between them. The numbers are still too small for satisfactory statistical analysis; but it does now look, according to Bahcall and Kellogg, as if there are two kinds of radio source associated with binary systems, one of which is a strong X-ray source and the other of which is not (see *Nature Physical Science* next Monday, August 27).

Perhaps it would be misleading to call these two kinds of source "classes", however, for of seven systems described by Bahcall and Kellogg six fall in one category and the other, HDE226868, stands alone. Although their calculations assume a thermal bremsstrahlung mechanism, the suggestion that there are two types of radio star (cool sources with $T \lesssim 10^7\text{ K}$ and HDE226868 sources with $T \sim 10^7\text{ K}$) is independent of that hypothesis. Some of the differences between the two categories are brought out in the figure, which compares the X-ray emission from Cyg X-1 (top), the X-ray counterpart of HDE226868, with the lack of X-ray emission from RY

Scuti (bottom). The possibility that the identification of HDE226868 with Cyg X-1 is wrong remains, of course, but, say Bahcall and Kellogg, "the present weight of evidence is strongly against this suggestion".



X-ray observations from Uhuru of Cyg X-1 (HDE226868, top) and the region of RY Scuti. The lack of X radiation from systems like RY Scuti suggests that these are fundamentally different from HDE226868.

magnetite is oxidized along 110 and 111 planes to thick ilmenite lamellae and contains spinel rods typical of oxidation classes IV or V. Thus there can be little doubt that the resulting palaeomagnetic data are reliable.

The mean palaeomagnetic direction from the fresh Wackerfield Dyke samples gives an ancient pole at 175° E, 22° N. This is only a few degrees from the pole obtained from Whin Sill samples by Storetvedt and Gidskehaug (*Phys. Earth planet. Int.*, **2**, 105; 1969) but is well removed from the Cleveland-Armathwaite Dyke pole reported by Giddings (thesis, University of Newcastle upon Tyne, 1969). It is true that Creer *et al.* (*Geophys. J.*, **2**, 306; 1959) obtained a palaeomagnetic direction from the Whin Sill which differed from the Storetvedt-Gidskehaug direction by 17° —and this makes the situation less clear than it would otherwise have been. Storetvedt and Gidskehaug argued, however, that the earlier result could be due to a stable, secondary post-Permian magnetization and noted that their own data agreed with other European data from samples of comparable age.

Tarling and his colleagues are clearly reluctant to arbitrate between the two Whin Sill results; but in view of the fact that the earlier direction was obtained from initial natural remanent magnetizations whereas samples used in the more recent study were demagnetized thermally and by alternating field, it is quite fair to say that the Storetvedt-Gidskehaug result is probably the most reliable. In any event, the Wackerfield Dyke pole is certainly well removed from the Tertiary Cleveland-Armathwaite Dyke pole, indicating that the Wackerfield Dyke cannot be Tertiary. And this is confirmed by a new radiometric age of 303 ± 5 million years of the Wackerfield Dyke. Tarling *et al.* thus conclude that, contrary to traditional belief, the Wackerfield Dyke is closely related to the Whin Sill. How many more such features remain wrongly identified?

CHEMISTRY

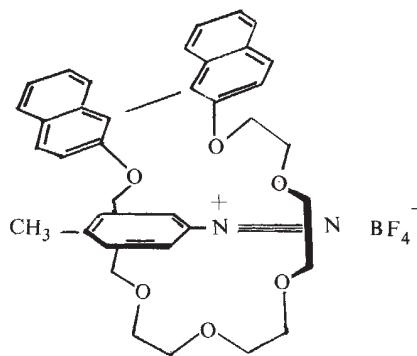
Round Peg in Round Hole

from our Chemical Physics Correspondent

CHEMISTS have for many years been intrigued with molecules of simple but unusual shapes, and examples of boats, chairs, crowns, sandwiches and so on are well known. So too are the solid clathrate materials in which guest molecules are held prisoner in a three-dimensional cage of the host, most often hydroquinone. Now Gokel and Cram (*J. Chem. Soc. Chem. Commun.*, 481; 1973) have provided an example of what may best be described as a peg in a hole, which forms in solution.

They find that a solution of 1 mol of

the crown-shaped molecule binaphtho-[20]crown-6-cyclic ether in chloroform will dissolve at least 0.9 mol of the peg, *p*-toluenediazonium tetrafluoroborate. This they attribute to the formation of the structure in the diagram. The solubility is indicative of some complex formation since the diazonium salt is normally insoluble in chloroform.



The proposed shape of the complex is supported by the finding that the slight modification of the crown to an open chain form destroys this unusual solubilizing ability. The structure is

further supported by nuclear magnetic resonance findings. The uncomplexed crown molecule has four particular hydrogens in the two Ar-O-CH₂- fragments, which are equivalent, or more strictly isochronous, and give rise to a set of lines due to spin-spin coupling that are all based on a single chemical shift, 4.06 p.p.m. When the diazonium salt is also dissolved these lines separate into two sets with chemical shifts of 3.89 and 4.06 p.p.m., showing that the protons are no longer all equivalent. The structure shown predicts this, as two of the protons are on the same side of the crown as the tolyl group and the other on the same side as the BF₄⁻ ion. The fact that the new spin-spin pattern is sharp implies that an individual peg must remain in its own hole for at least a second.

At first sight this set of plugged holes floating in the bathwater may seem to be only a curiosity. But it has already been shown that the efficiency of the solubilization process is a sharp function of ring size and peg shape, so that quite sophisticated fractional extractions might be possible.

Magnetic Properties of Exposed Oceanic Crust

In spite of the important part played by oceanic magnetic anomalies in global tectonic theory, the nature and form of the magnetic source or sources in oceanic layer 2 remain obscure. But a little experimental evidence is available. For example, Marshall and Cox (*Bull. geol. Soc. Am.*, **82**, 537; 1971) recently showed that a layer of extrusive rock (pillow lava) less than 1 km thick could account for observed anomaly amplitudes if the high intensity natural remanent magnetizations (NRMs) found in their dredged samples were to obtain throughout the layer. High NRM intensities have also been found in samples of pillow lava dredged from the mid-Atlantic ridge, although the reduction in anomaly amplitude away from ridges suggests that high intensities are not universal, possibly because pillow lavas easily undergo low temperature oxidation. Lower NRM intensities in older oceanic crust have also been observed directly by drilling into layer 2.

But this is only touching the surface, both literally and figuratively — what is really required to solve the problem is the ability to drill right through the oceanic crust, or at least through layer 2. Such complete sampling is not yet feasible for the present oceanic crust but is possible for formations such as the Troodos ophiolite complex of Cyprus which are thought to be upthrust sections of ancient oceanic crust. Another example is Macquarie Island which was almost certainly formed during the late Tertiary at the active Australia-

Antarctica ridge; and as Butler and Banerjee showed in last Monday's *Nature Physical Science* (August 20), ancient oceanic crust such as Macquarie Island can have magnetic properties quite different from those of young dredged samples.

The Macquarie materials investigated by Butler and Banerjee included pillow lavas, basaltic and doleritic dykes, gabbro and serpentinized harzburgite. The first important point to emerge from the study was that the pillow lavas had NRM intensities at least an order of magnitude lower than those of young pillow lavas. Their stability to alternating field demagnetization was also lower. These results are entirely consistent with the view that pillow lavas gradually undergo low temperature oxidation or low grade metamorphism; but whatever the cause of the lower NRM intensities, it is clear that the contribution to the observed anomalies from pillow lavas must decrease with age.

The basaltic and doleritic dykes, on the other hand, were found to be much more stable magnetically than the lavas; and their NRM intensities were high enough to suggest that they may make a significant contribution to the observed anomalies. Moreover, even the gabbroic and ultramafic intrusive layer cannot be entirely rejected as a magnetic source, for the gabbro has an unusually high NRM intensity and stability for an intrusive rock. In short, "the ability to produce magnetic anomalies is not limited to the pillow lava layer".

Organic Ionic Melts

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Professor Ubbelohde describes recent work on a novel class of liquids—organic molten salts.

TRADITIONALLY, work on the liquid state has dealt mostly with molecules whose repulsive and attractive forces are short range. Even computer models overemphasize "hard sphere" short range forces in the liquid state. Yet when liquids are considered by reference to the types of crystal compound from which they are formed on melting¹, more than one novel class of liquid warrants special attention. As one example, liquids with long range forces between the molecule include many molten salts. With inorganic molten salts, the physical chemistry is becoming better known; and for several years, I have endeavoured to enlarge this class of liquids to include organic molten salts. These have the theoretical attraction that a family of salts might be studied, for example, with a structurally related series of acids in which there are only small differences of structure. This might permit sensitive tests of various theoretical aspects of the liquid state.

One serious and quite general difficulty had to be overcome at the outset of work on organic molten salts. Many of these are relatively stable in crystalline form, but even when their melting points are low and the organic structures simple, it was surprising that the liquids obtained on melting often showed much enhanced chemical instability.

At first, it was not known if this general finding might be due to intrinsic changes in the micro-environment of the ions on passing from the crystal lattice to the molten state². Alternatively, greater instability of the melts might arise from impurities whose molecular freedom of movement is enhanced in the liquid. Recent reaction kinetic studies in organic ionic melts have revealed many suggestive features in favour of the second possibility, and have shown that by carefully excluding certain impurities³⁻⁵ crystalline salts can be prepared that give organic ionic melts indefinitely stable up to about 350° C. These novel liquids are now available for precise studies, as well as for bulk uses, for example in engineering or optical applications.

Some novel aspects may be illustrated by reference to alkane carboxylates with one of the cations Li, Na, K, Rb or Cs. Acid anions of general formula $C_nH_{2n+1}CO_2^-$ were chosen with $n \leq 6$ to concentrate attention on organic ionic melts in which the ratio of the charge to the total number of atoms is still quite large, leading to characteristic ionic liquids in which the electrostriction is still high. Many other kinds of organic ionic melts with less electrostriction can, of course, also be studied.

Two-stage Melting

Transition to a "liquid" on melting a "crystal" can be characterized either by thermodynamic or non-thermodynamic (such as mechanical) criteria¹. With crystals of

complex structure, "melting points" defined in these alternative ways may show significant discrepancies. Usually, it is best to identify melting points thermodynamically.

With others, I have determined stable liquid ranges for this novel class of liquids using a scanning calorimeter⁶, as well as dilatometry^{7,8}. For all five alkali cations, salts with anions up to $n=3$ give conventional ionic melts with a useful liquid range, seldom less than 100° C. But for $n>3$, a novel feature appears, in that a first melting transition occurs at T_1 to a mesophase birefringent state. Organic ionic melt mesophases resemble more familiar "liquid crystals" of organic chemistry, except for the stronger and longer range electrostatic forces acting between their molecules. When an organic ionic crystal gives a mesophase at T_1 , it passes into a clear ionic melt at higher temperatures (T_{cl}).

Mechanical Mechanisms of Melting

As an alternative to thermodynamic descriptions, a liquid is sometimes defined mechanically as a condensed state of matter incapable of withstanding applied shear stress. On this basis, our recent studies suggest that organic ionic melt mesophases are probably better described as extremely plastic solids, with elastic limits so low that they would be missed in conventional observations. For shear stresses exceeding these limits, once flow starts, mechanical properties may alter because of molecular orientation induced by flow. To study this kind of memory effect, a relaxometer has been designed and constructed in which the forces applied can be as low as 30 nN with shear stresses as low as 0.1 nN m⁻². Although still in early stages of design, this instrument⁹ confirms very low elastic thresholds, passing into continuous flow above about 55 nN m⁻². Although flow is not strictly Newtonian, viscosities, measured in conventional capillary viscometers, are about 100 poise for sodium-*n*-isovalerate in its mesophase, dropping to about 0.1 poise above the second melting point, T_{cl} .

Texture and Properties

For characteristic examples of these crystals, entropies of fusion are below 3 e.u. and the jump in electrical conductance on melting is exceptionally small⁶. These pointers to a close similarity of molecular arrangements in crystals and melts are confirmed by optical and X-ray studies¹⁰. Optical studies of birefringence indicate relatively large domains extending over 100 μ m in molten sodium-*n*-butyrate and over a few millimetres in molten sodium isovalerate. X-ray measurements over a range of temperatures traversing the first melting point T_1 and the second melting point T_{cl} show that these domains contain stacks of parallelized electrostatic sandwiches rather like striped serpents (Fig. 1b). Single electrostatic sandwiches (Fig. 1a) are formed by pairs of alkane carboxylate layers in opposition.

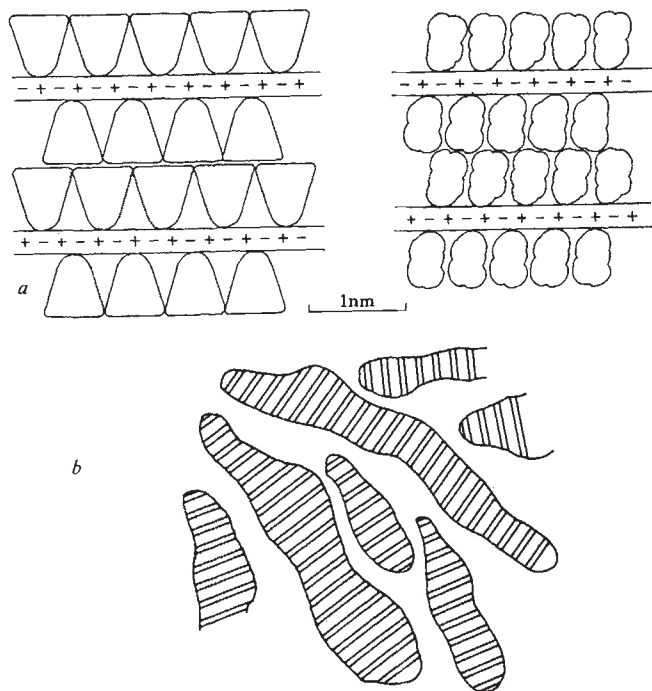


Fig. 1 *a*, Scale diagram of space occupied by anions (repulsion envelopes) packed between cation (+) and carboxyl (-) electrostatic sandwiches. Left, sodium butyrate; right, sodium isovalerate. *b*, Domains of stacked electrostatic sandwiches in organic ionic melt mesophases.

In each sandwich, alkane anions are under strong electrostrictive forces from the layers of electrostatic charges. This leads to remarkable thermal behaviour as the temperature of the mesophase is raised from T_i to above the clearing temperature T_{cl} . In sodium isovalerate, for example, zero thermal expansion is observed normal to the electrostatic layers, over a temperature interval of some eighty degrees, whereas in sodium-*n*-butyrate the electrostatic layers shrink closer together as the temperature is

raised. Because the total volume of each of these mesophase melts increases normally with temperature, this implies that the domains (and the more disordered fluid between them) must expand laterally as the temperature rises, up to the clearing point T_{cl} at which the liquid passes into a more normal ionic melt arrangement.

Ionic Melt Liquid Crystals

In recent years interest in molecular "liquid crystals" has flared up to a remarkable extent. This has been stimulated by potential technical applications of effects of applied magnetic and electrical fields in optical and other physical properties of these "liquids"¹¹⁻¹⁵. Preliminary measurements (with J. J. Duruz) indicate that some of the phenomena already identified with molecular "liquid crystals" take distinctive forms in organic ionic melt mesophases. Because these novel ionic fluids have now become available at moderate cost in considerable bulk, the range of "liquid crystal" phenomena which can now be studied in the laboratory and possibly used for practical applications has been considerably extended.

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Sensitivity in the World Dynamics Model

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A computer analysis of Forrester's World Dynamics Model shows that the model is very sensitive to the input assumptions with respect to capital investment and pollution. An algebraic description of the model and six considerations basic to such a simulation are also presented.

I SHALL try to illuminate the extensive discussion of Forrester's simulation of the world¹⁻⁹ in three ways; by giving a description of the World Dynamics Model in standard algebraic notation rather than the specialized Dynamo notation, by presenting the results of a sensitivity analysis of the model,

and by noting some of the fundamental considerations inherent in this kind of simulation.

I find that the World Dynamics Model is very sensitive to the input assumptions: the change of any one of several values produces large changes in the curves of population, pollution and natural resources. These results point in one of three directions: either the world is indeed sensitive to small changes in the input descriptors; or the World Dynamics Model is basically a correct description of the world, but it requires a more accurate set of inputs (Tables and constants); or the model has serious flaws and requires extensive re-examination.

Logic of the Model

The World Dynamics Model is a program written in the Dynamo language. I describe the program in algebraic notation in the Appendix to this article.

The model is based on two central assumptions; that the world can be adequately described in terms of five state variables (population, capital investment, pollution, agriculture and natural resources), and that these variables, with twelve intermediate ones, can be defined by twenty-two Tables or graphs (see Appendix). The Tables are not based on any statistical analysis (ref. 1, chapter 3); nonetheless, Forrester states that "the model asserts that the relationships chosen for inclusion are important, that the omitted relationships are less important, and the 'real-world' interactions can be represented usefully as described in the details of the model. . . ." He goes on to suggest (ref. 1, pages 31, 32) that, because of this, "the reader should examine the assumptions and relationships for plausibility and . . . he would want . . . to determine which changes in assumptions result in significant changes in system behavior . . .".

I have found that "significant changes in system behavior" occur if one point in one of three Tables (CMT, POLCMT, or POLATT) is changed, if one of two constants (CIGN or CIDN) is changed, or if the growth mechanism in one state variable (population) is modified.

Sensitivity Analysis

I have made more than sixty runs of the World Dynamics Model using the Dynamo compiler and the exact program presented in *World Dynamics*¹. These runs examined three aspects of the model: capital investment, pollution, and exponential growth with respect to population.

In the Forrester model, the capital investment increment is given by the difference between capital investment generated (CIG) and the capital investment discarded (CID). Thus

$$CI(t+\Delta t) = CI(t) + (CIG - CID)\Delta t \quad (4)$$

(Equation numbers correspond to those in the Appendix.) Capital investment generated is the product of three factors: the capital investment generation constant (CIGN), the capital investment multiplier which is a function of mean standard of living, CMT (MSL), and population, $P(t)$; thus

$$CIG = CIGN [CMT (MSL)]P(t) \quad (2)$$

Capital investment discarded is the product of two factors; the capital investment discard constant (CIDN) and the capital investment $[CI(t)]$; thus

$$CID = [CIDN]CI(t) \quad (3)$$

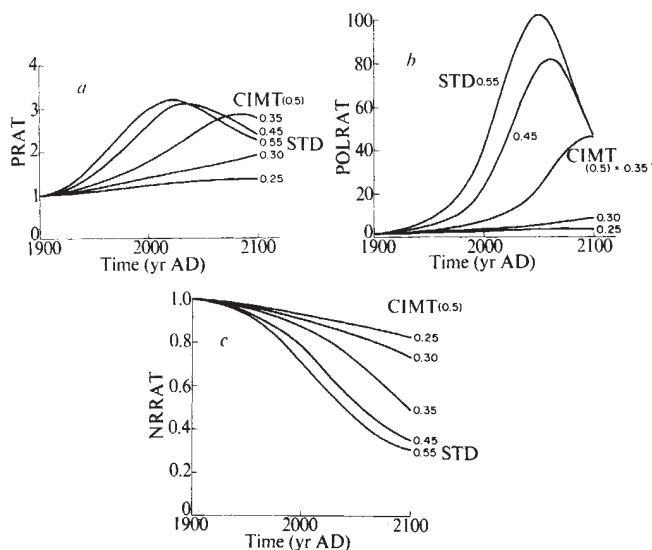


Fig. 1 Effect of varying CIGN (0.5). Time variation of, a, normalized population (PRAT); b, normalized pollution (POLRAT); c, normalized natural resources remaining (NRRAT).

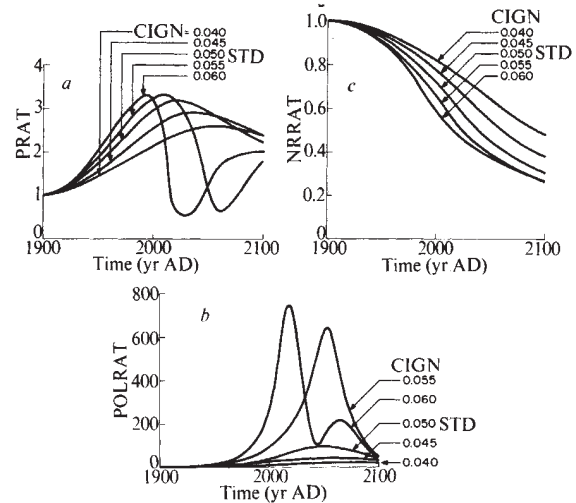


Fig. 2 Effect of varying the capital investment growth normal (CIGN). Time variation of, a, normalized population (PRAT); b, normalized pollution (POLRAT); c, normalized natural resources remaining (NRRAT).

The sensitivity analysis reported here examined the capital investment equations by varying CIGN (0.5) over the range 0.25 (0.05) 0.55 (Fig. 1), CIGN over the range 0.040 (0.005) 0.060 (Fig. 2), and CIDN over the range 0.015 (0.005) 0.030 (Fig. 3).

Each of Figs 1-3 shows relative population, PRAT, relative pollution, POLRAT, and relative natural resources remaining, NRRAT. In each case, the variable is the value of relevant state variable at time, t , divided by the state variable value at $t=1900$. Further, in each figure, the curve labelled STD is the one produced by the exact program presented in ref. 1.

Briefly, as one point of the capital investment multiplier table, CMT (0.5), is reduced from the standard value (Fig. 1), population and pollution increases are substantially reduced, and natural resources remaining are substantially increased. When the capital investment generation constant is varied from 0.040 to 0.060, maximum population and maximum pollution increase appreciably, the variables becoming oscillatory for the larger values of CIGN, and the natural resources remaining are substantially decreased. The result of decreasing the capital investment discard constant (Fig. 3) CIDN is similar to that produced by increasing CIGN.

This last result is especially interesting, because it states that increasing the capital investment generation constant has the same general effect as decreasing the capital investment discard constant. Why this happens in the model is clear from equation (4). Increasing CIGN or decreasing CIDN has the effect of increasing the capital investment increment. Whether this behaviour corresponds to that in the real world is another question.

In addition to the sensitivities shown in Figs 1-3, I examined the effect of varying one point in each of the two pollution Tables: POLCMT (2.0) over the range 2.0 (0.5) 4.5 and POLATT (0) over the range of 0.1 (0.1) 0.7. By varying the one point in either one of these Tables, the maximum pollution was increased by a factor of 4 over the standard case.

S-Shaped Growth

"Examples of growth systems," according to Kaysen, "are known that display quite different behaviour as they approach their natural limits than the sharp reversals portrayed in *Limits*. For instance, a system in which the rate of growth of the major variables was proportional to their distance from their limit would show a smooth, gradual, stable adaptation to its growth ceiling" (ref. 2, page 661). This comment was examined briefly with regard to population by introducing a

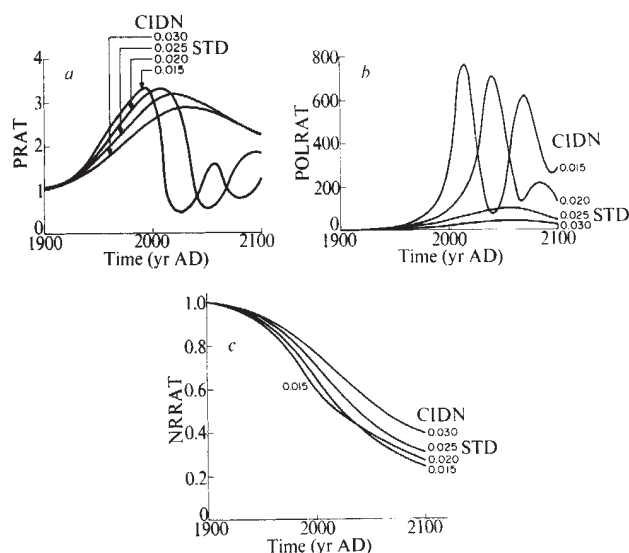


Fig. 3 Effect of varying the capital investment discard normal (CIDN). Time variation of, *a*, normalized population (PRAT); *b*, normalized pollution (POLRAT); *c*, normalized natural resources remaining (NRRAT).

factor $[1-P(t)/PMAX]$ into equation (1). Whereas that equation states population is determined by

$$P(t+\Delta t) = P(t) + \Delta t[BR - DR], \quad (1)$$

I modified this to

$$P(t+\Delta t) = P(t) + \Delta t[BR - DR] [1 - P(t)/PMAX], \quad (1a)$$

where the new factor was applied only for time greater than 1970. Before 1970, which may be regarded as the "awareness time", equation (1) was used. The growth mode defined by equation (1a) is here called "S-shaped growth". Because this modification reduces the population increment more as the population approaches an assumed maximum, PMAX, it may simulate the fact that as people become more aware of a problem, in this case overpopulation, they will apply various kinds of constraints.

In these runs, PMAX was varied from 1.5 to 5.0 times the 1900 population (PI) in increments of 0.5. The standard model corresponds to PMAX infinite. Briefly, as PMAX/PI was increased from 1.5 to 5.0, the peak population (PRAT) increased by 30%, the peak pollution (POLRAT) decreased by 100%, the NRRAT remaining in 2100 increased by 0.3%, and the peak normalized capital investment decreased by 1.5%. In other words, a substantial change in population was accompanied by a negligible change in capital investment and natural resources. Another interesting result was the decrease in pollution as the population increased.

Of course, the same technique to simulate S-shaped growth can be applied to the other state variables, and the "awareness times", 1970 in equation (1a), can be independent for each variable. A possible way of applying the "awareness" concept to capital investment might be to allocate different fractions of capital investment to specific problems, for example, pollution or natural resources, with the fraction determined by how close the world has come to a preset limit.

Conclusions on Parameter Variations

Clearly, the model is sensitive to the input assumptions, especially so with respect to those about capital investment and pollution. It is also noteworthy that population is very sensitive to capital investment changes while capital investment is relatively insensitive to population. Some of the variables show a pronounced tendency to oscillate, such as popu-

lation in Figs 2a and 3a and pollution in Figs 2b and 3b. These results concerning sensitivity point in one of three principal directions: either the World Dynamics Model is basically a correct description of the world, but requires a more accurate set of inputs (Tables and constants); or the world is indeed very sensitive to small changes; or the model has serious flaws and requires extensive re-examination. As noted below, which direction is the more appropriate cannot be determined from within the simulation.

Fundamental Considerations of the World Dynamics Model

I shall now discuss six considerations that are central to an understanding of the World Dynamics Model, and indeed to any attempt to simulate the world. These go beyond the question of a particular Table or a particular constant.

(1) The Axiom-Logic System: The World Dynamics Model is a closed mathematical system with its own axioms and its own logical structure and must be examined as such. The Tables and constants constitute the axioms, and the equations constitute the logical structure. The pollution crisis N yr later, for example, is built into the assumptions of the model even though this is not apparent because of the model's complexity. There is a close parallel between this situation and that of Euclidean geometry where the Pythagorean theorem is built into the set of axioms and the logic. There is no more convincing proof of this than the geometries of Riemann and Lobachevski, where, by changing one Euclidean axiom, these men produced completely different geometries. The fact that we find Euclidean geometry useful in many practical applications is fortuitous, but the justifications for these applications certainly do not follow logically from Euclid's closed mathematical system. In a similar sense, any relationship between the results of the World Dynamics simulation and the situation in the real world has to be established and argued outside the simulation. The most one can hope for is that use of the model may inform and illuminate the search for an understanding of the world situation.

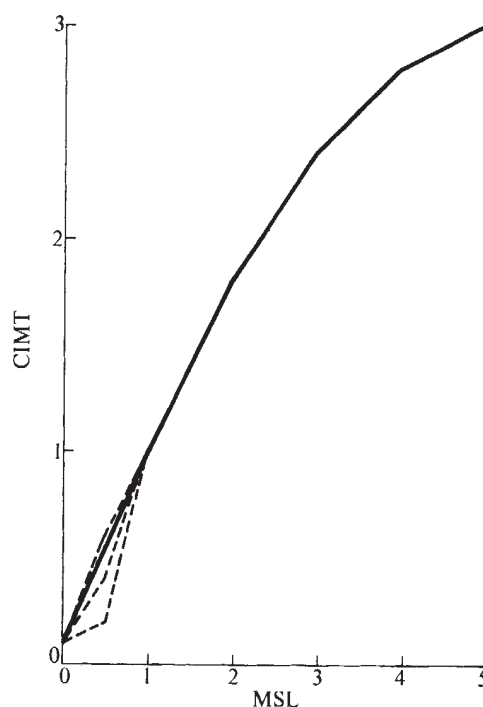


Fig. 4 Capital investment multiplier (CIMT) as a function of mean standard of living (MSL). ---, Effect of changing the value of CIMT (0.5). All curves are identical for MSL greater than 1.

(2) Spatial Homogeneity: Many commentators have noted that the level of aggregation in Forrester's simulation is too high, that describing the capital investment policy of the world—the Western world, the Socialist world, and the underdeveloped world—in one equation cannot lead to useful results. The results given above about the sensitivity of the capital investment equations give point to this concern. One could argue that a low capital investment multiplier for a low material standard of living is a reasonable description of an uncontrolled, underdeveloped economy, but a very poor description of a highly controlled economy. What multiplier would be appropriate for a developed, partially controlled economy is still another relevant question. Indeed, is a single capital investment multiplier Table a useful concept?

(3) Temporal Homogeneity: The World Dynamics simulation makes the fundamental assumption that a tabular relationship, at best determined with data available up to time t , is valid for all future time. Because these Tables must in some way include the integrated effects of many changes in transportation, energy, birth control, communications, social systems, to mention just a few, it is difficult to imagine that equally competent investigators would choose the same Table of values for each variable in 1900, 1971, or 2042. But the sensitivity analysis shows that these choices are critical to the outcome. The assumption that Tables can be valid for more than a century after the relevant data were collected asserts a greater understanding of human dynamics than most social scientists claim.

(4) Identification of State Variables: The identification of the state variables and the factors that will enter into their computation is as crucial in the World Dynamics simulation as in any simulation. Would a competent investigator in 1900 have identified pollution as a major variable for the next 200 yr? Is it possible that the amount and control of thermonuclear fuel will be the crucial variable 100 yr hence? Although the choice of state variables in the World Dynamics Model may seem reasonable today, one would probably want more support before committing the simulation to these five exclusively. It would be interesting to examine what factor analysis and other statistical methods can contribute to the choice of variables and their relative weights.

(5) Modes of Growth: A further consideration is that population in the World Dynamics Model is based on the difference equation of exponential growth

$$P(t + \Delta t) = P(t) + K[P(t)]\Delta t$$

where K is a function of time and other variables. As has already been suggested by Kaysen, there are other growth mechanisms, and I have illustrated at least one such. It would be interesting to learn what justification one could adduce for different growth mechanisms. In any case, the equations of growth are important to a simulation of the world, and they should bear a good deal of scrutiny in any model.

(6) Accuracy of Data: Finally, the World Dynamics Model admittedly is not based on detailed world data, so it may not be fair to criticize it because it happens to be sensitive to some input assumptions. But the analysis does suggest accuracy levels that should be met if one accepts the model. Additionally, if the accuracy requirements turn out to be great, one may be confronted with definitional problems. This is a frequent consequence of more precise measurements of more extensive data requirements.

I thank E. L. Kay and S. E. Rose for encouragement.

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Appendix

This appendix contains, in algebraic notation, a description of the World Dynamics Model program (ref. 1, pages 132–137). Whereas that program used 111 symbols or variable names, the following description does not contain so many because many of them are, in some sense, duplicates, some are control variables, and some are not used in the standard model.

In the following description, which contains the exact substance of the standard model, four notational elements are used. (a) A set of contiguous letters constitutes a variable name (for example, MSL is material standard of living, BR is birth rate and so on). (b) Brackets are used to indicate multiplication. (c) Variable names ending in "T" refer to Tables used in the model (such as CIMT, the capital-investment-multiplier Table). (d) Parentheses are used to indicate functional notation. Thus NRMST (MSL) is the ordinate in the NRMST Table corresponding to the independent variable MSL. The tables used by Forrester are defined in the program; graphs and justifications for the Tables are given in *World Dynamics* (ref. 1, chapter 3).

Set Initial Conditions

Time step of simulation, $DT = 0.2$ yr
Initial population, $PI = 1.65 \times 10^8$ people
Initial capital investment, $CII = 4 \times 10^8$ units
Initial pollution, $POLI = 2 \times 10^8$ units
Initial capital-investment-in-agriculture-fraction, $CIAFI = 0.2$
Initial natural resources, $NRI = 9 \times 10^{11}$ units
Time, $t = 0$

Calculate the Independent Variables

$NRFR = NR(t)/NRI$
 $NREM = NREMT(NRFR)$
 $CIR = CI(t)/P(t)$
 $MSL = CIR[1 - CIAF(t)]NREM/0.7$
 $POLR = POL(t)/(3.6 \times 10^9)$
 $FPM = FPMT(POLR)$
 $CR = P(t)/(1.35 \times 10^8 \times 26.5)$
 $FCM = FCMT(CR)$
 $CIRA = CIR[CIAF(t)]/0.3$
 $FPCI = FPCIT(CIRA)$
 $FR = [FPCI][FCM][FPM]$
 $QLM/QLF = QLMT(MSL)/QLFT(FR)$

Calculate Population

$BR = 0.04 P(t)[BRCMT(CR)][BRFMT(FR)]$
 $[BRMMT(MSL)][BRPMT(POLR)]$
 $DR = 0.028 P(t)[DRCMT(CR)][DRFMT(FR)]$
 $[DRMMT(MSL)][DRPMT(POLR)]$
 $P(t + DT) = P(t) + DT[BR - DR] \quad (1)$

Calculate Capital Investment

$CIGN = 0.05$
 $CIDN = 0.025$
 $CIG = [CIGN][CIMT(MSL)]P(t) \quad (2)$
 $CID = [CIDN]CI(t) \quad (3)$
 $CI(t + DT) = CI(t) + DT[CIG - CID] \quad (4)$

Calculate Pollution

$POLG = [POLCMT(CIR)]P(t) \quad (5)$
 $POLA = POL(t)/[POLATT(POLR)] \quad (6)$
 $POL(t + DT) = POL(t) + DT[POLG - POLA] \quad (7)$

Calculate Capital-Investment-in-Agriculture-Fraction

$$\text{CIAF}(t + \text{DT}) = [1 - \text{DT}/15]\text{CIAF}(t) + [\text{DT}/15][\text{CFIFRT}(\text{FR})] [\text{CIQRT}(\text{QLM}/\text{QLF})] \quad (8)$$

Calculate Natural Resources

$$\text{NR}(t + \text{DT}) = \text{NR}(t) - \text{DT}[\text{NRMMT}(\text{MSL})]P(t) \quad (9)$$

Calculate Quality of Life

$$\text{QL}(t) = [\text{QLMT}(\text{MSL})][\text{QLCT}(\text{CR})][\text{QLFT}(\text{FR})] [\text{QLPT}(\text{POLR})] \quad (10)$$

Increment time by DT

Go to "Calculate the Independent Variables"

When simulation is complete, print and plot results

Definition of Symbols

BR	Birth rate (people yr^{-1})
BRCMT	Birth rate from crowding multiplier Table
BRFMT	Birth rate from food multiplier Table
BRMMT	Birth rate from material multiplier Table
BRPMT	Birth rate from pollution multiplier Table
CFIFRT	Capital fraction indicated by food ratio Table
CI	Capital investment (capital units)
CIAF	Capital investment in agriculture fraction (dimensionless)
CIAFI	Capital investment in agriculture fraction, initial (dimensionless)
CID	Capital investment discard (capital units yr^{-1})
CIDN	Capital investment discard normal (fraction yr^{-1})
CIG	Capital investment generation (capital units yr^{-1})
CIGN	Capital investment generation normal (capital units per person yr^{-1})
CII	Capital investment, initial (capital units)
CIMT	Capital investment multiplier Table
CIQRT	Capital investment from quality ratio Table
CIR	Capital investment ratio (capital units per person)
CIRA	Capital investment ratio in agriculture (capital units per person)
CR	Crowding ratio (dimensionless)

DR	Death rate (people yr^{-1})
DRCMT	Death rate from crowding multiplier Table
DRFMT	Death rate from food multiplier Table
DRMMT	Death rate from material multiplier Table
DRPMT	Death rate from pollution multiplier Table
FCM	Food from crowding multiplier (dimensionless)
FCMT	Food from crowding multiplier Table
FPCI	Food potential from capital investment (food units per person yr^{-1})
FPCIT	Food potential from capital investment Table
FPM	Food from pollution multiplier (dimensionless)
FPMT	Food from pollution multiplier Table
FR	Food ratio (dimensionless)
MSL	Material standard of living (dimensionless)
NR	Natural resources (natural resource units)
NREM	Natural resource extraction multiplier (dimensionless)
NREMT	Natural resource extraction multiplier Table
NRFR	Natural resource fraction remaining (dimensionless)
NRI	Natural resources, initial (natural resource units)
NRMMT	Natural resource from material multiplier Table
P	Population (people)
PI	Population, initial (people)
POL	Pollution (pollution units)
POLA	Pollution absorption (pollution units yr^{-1})
POLATT	Pollution absorption time Table
POLCMT	Pollution from capital multiplier Table
POLG	Pollution generation (pollution units yr^{-1})
POLI	Pollution, initial (pollution units)
POLR	Pollution ratio (dimensionless)
QL	Quality of life (satisfaction units)
QLCT	Quality of life from crowding Table
QLF	Quality of life from food (dimensionless)
QLFT	Quality of life from food Table
QLM	Quality of life from material (dimensionless)
QLMT	Quality of life from material Table
QLPT	Quality of life from pollution Table
TIME	Calendar time (yr)

Positional Information in Chick Limb Morphogenesis

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Pattern formation by the cells of a growing organism depends on coordination of changes in space and time. Evidence is presented here for the control of morphogenesis by positional information specified by an autonomous timing mechanism that operates in a "progress zone" at the tip of the limb bud.

SPATIAL patterns of cellular differentiation may be established by a two step process: the cells may first have their positions specified with respect to certain boundary or reference

regions, as in a coordinate frame, and may then interpret this positional information by selecting an appropriate course of differentiation, according to their genome and developmental history^{1,2}. The idea of positional information has so far been applied principally to regulative systems such as insect epidermis³ and *Hydra*⁴, where growth is not a prominent feature. For these systems some quite successful models have been developed, involving two gradients, one in a diffusible substance, acting as a signal of position, and another in a more stable cell parameter which may be considered as an intrinsic positional value. The diffusible signal gradient may be maintained, for example, by a source at one boundary and a sink at another⁵. The models embody rules for the interaction between the two gradients.

Here we show how positional information may be assigned and used to pattern a growing organ, the embryonic chick limb. The mechanism is different from those mentioned

above, according to which cells read positional information from the local value of a position-dependent signal. Just as navigation can depend on clocks as well as maps, so the intrinsic positional character of cells and tissues may be decided by a combination of spatial and temporal cues. In particular, specification by timing can supplant specification by a graded signal maintained by localized sources and sinks. This is especially true for patterns laid down in the course of growth.

For example, as the limb grows out and lengthens, the more and more distal positional values may be allocated just behind its advancing tip at later and later times. The tissue at the very tip can, through growth, serve as a source of the new distal territories, while its own positional character remains in a state of flux. The tissue that emerges early from the labile tip region, in this type of outgrowth, will be proximal; the tissue that emerges late will be distal. The positional character of a group of cells may therefore be decided by the length of time that they or their ancestors have spent in the labile tip region. Some spatial signal is needed to mark out the extent of that region, but this is the only cue that the surrounding tissues must supply to generate the proper proximo-distal sequence of parts. There is no need for an external signal to specify positional value. The specification may, instead, depend entirely on the timing of the stay in the labile region, if there, and only there, tissue changes spontaneously to become steadily more distal in its intrinsic character.

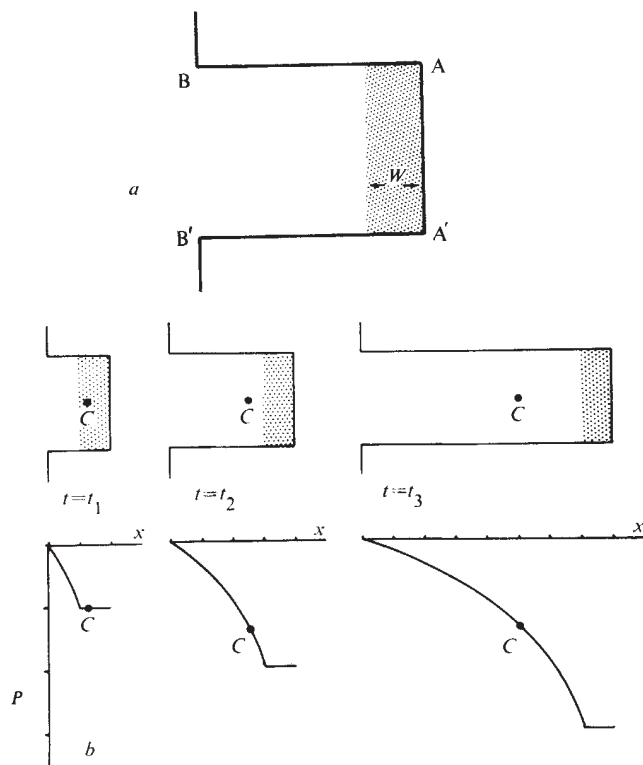


Fig. 1 *a*, An idealized outgrowth. BB' is its base, and AA' is its tip. The progress zone, of width W , is marked by shading. *b*, The positional value P is shown as a function of the distance x from the base of the idealized outgrowth at three successive times, t_1 , t_2 , t_3 . C marks the mean position of one typical cell lineage followed through the three ages. Inside the progress zone, P is taken to change at a rate proportional to the rate of cell proliferation, while elsewhere P is fixed so that the pattern of positional values can only spread out by interstitial growth. Note that the size of the progress zone governs the size of the structures that emerge. If the zone were reduced to half its normal width, the full normal range of positional values would initially be crammed into only half the normal expanse of tissue: each anatomical rudiment would be only half its normal length.

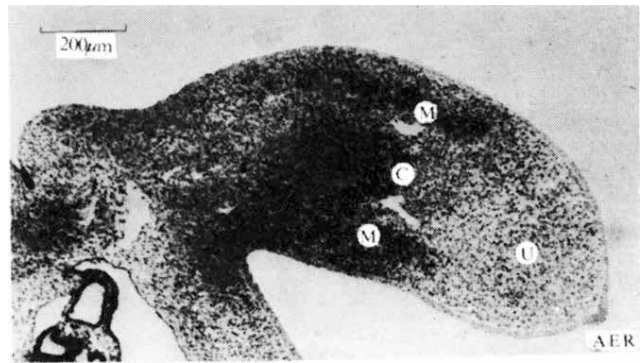


Fig. 2 A stage 23 chick wing bud sectioned in the plane of the proximo-distal and dorso-ventral axes. (Fixed in Karnovsky's fixative, embedded in 'Araldite', cut at $1\ \mu\text{m}$, and stained with toluidine blue.) AER, apical ectodermal ridge; U, undifferentiated tip mesenchyme; M, pre-muscle; C, pre-cartilage.

If the rate of this spontaneous change is proportional to the rate of cell division in the labile region, then the assignment of positional values will always be harmoniously linked with growth; the pattern will be tailored to the size of the system at every stage. This is an important consideration for almost all embryos, both plant and animal, whose growth may often be hastened or delayed by chance variations of temperature. There is some direct evidence that cells in a different type of system, an insect epidermis³, can change their intrinsic positional value only when they divide. In the type of outgrowth described here, cell division may continue outside the labile region, but there it will not be associated with a change of positional value. A labile region where new positional values are successively engendered in the course of growth, we shall call a "progress zone". For an idealized system (Fig. 1*a*) growing out uniformly along one axis with a progress zone at its tip, we obtain, at successive times, the patterns of positional value shown schematically in Fig. 1*b*.

We shall now argue that the embryonic chick limb does in fact develop by such a mechanism. We shall consider only the proximo-distal organization. There is substantial evidence that the antero-posterior coordinate of positional value is specified in a different way, involving some kind of signalling from a polarizing region close to the posterior border of the limb bud^{1,6}; very little is known about the dorso-ventral axis.

The Chick Wing

The chick wing bud starts as a very small bulge from the flank, and grows out as a tongue-shaped mass, consisting of mesenchyme encased in ectoderm. The ectoderm is even and featureless, except for the apical ectodermal ridge, a thickening running round the distal rim of the bud. Earlier work has emphasized the interactions between the mesenchyme and this ectodermal ridge in relation to limb outgrowth⁶⁻⁸. We have suggested that the overall shape of the limb bud may depend on the mechanics of the ectoderm and in particular on the strengthening role of the apical ridge⁹.

We wish here to focus attention on the mechanism by which the skeletal elements along the proximo-distal axis are specified, each with its own distinctive character. These are laid down within the mesenchyme in a proximo-distal sequence¹⁰: the primordia of proximal structures begin to differentiate first, while the primordia of more distal structures appear at successively later times and more distal positions. But the tip, that is, the layer of mesenchyme extending inwards from the apical ridge for about $400\ \mu\text{m}$, remains apparently undifferentiated up to stage 28 or so (Fig. 2), and continues to proliferate relatively rapidly¹¹. We find autoradiographically that all the cells there are

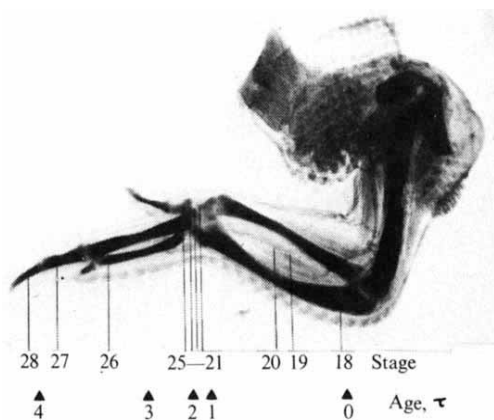


Fig. 3 The mean level of truncation is shown following apical ridge excision at each of the stages indicated. The mean for each stage is derived from measurements of at least seven cases. Beneath the stage numbers we mark the estimated age τ defined as the number of cell divisions that have elapsed in the tip mesenchyme since stage 18, when the limb bud first begins to bulge out. Note the bunching of results at the wrist. This is due to a relatively high cell density and low proliferation rate in that region after it emerges from the apical zone (D. S. and J. H. L., unpublished). The truncated limbs and contralateral controls were fixed in 5% TCA at 9–10 d incubation, stained with alcian green, and cleared in methyl salicylate for measurement.

actively dividing; the distal cells have been reported also to preserve a “morphogenetic potential” at stages when proximal cells have already lost it¹². We suggest that there is a progress zone located within this mesenchyme beneath the apical ridge, that is, the tip of the limb bud is a region of change, generating tissue with new and progressively more distal positional values. These positional values are interpreted by the cells to give the sequence of distinctive structures.

Removal of the Apical Ridge

A classical experiment of Saunders¹⁰ shows that the lability of the tip mesenchyme depends on the presence of the apical ectodermal ridge. Saunders found that if the apical ectodermal ridge is cut off, the limb fails to develop distal elements: it is normal up to a certain level beyond which there is nothing. The later the stage at which the ridge is removed, the more nearly complete the resulting limb. Conversely, when a supernumerary ridge is grafted onto the dorsal surface of a limb bud, a secondary distal axis develops beneath it⁶. We have repeated and extended (D. S. and J. H. L., unpublished) Saunders's series of experiments of the former type with a view to providing more quantitative data, and have measured the lengths of the various skeletal elements, using the undisturbed side as control¹³.

In Fig. 3 we show the cut-off level following apical ridge removal between stages 18 and 28. In the terms of our theory, apical ridge removal halts the change of positional value in the apical mesenchyme: when the ridge is removed progress stops in the zone at the tip. The cells there lose their lability prematurely, reduce their rate of proliferation, and start to differentiate according to their current positional value. The resulting limb is therefore shorter, lacking not only the most distal positional values, but also the cells which would have expressed them.

By excising the apical ridge, we assay for the positional value at the tip. If, for example, we halt all changes of positional value at stage 22, and obtain a limb truncated at the wrist, the most distal positional value in the stage 22 limb bud must have been that corresponding to the wrist. The assay is, however, marred by two uncertainties; we do not know accurately the extent of trauma, nor how promptly the positional value stops changing after the apical ridge is removed. Disregarding this correction, we can now re-

interpret Fig. 3; it shows, for each stage, S , from 18 to 28, which eventual limb structure has the same positional value as stage S tip tissue. We can use it in conjunction with presumptive fate maps to deduce the width of the progress zone. Our analysis gives $300 \pm 100 \mu\text{m}$ as a rough estimate (D. S. and J. H. L., unpublished).

Grafting of Distal Tips

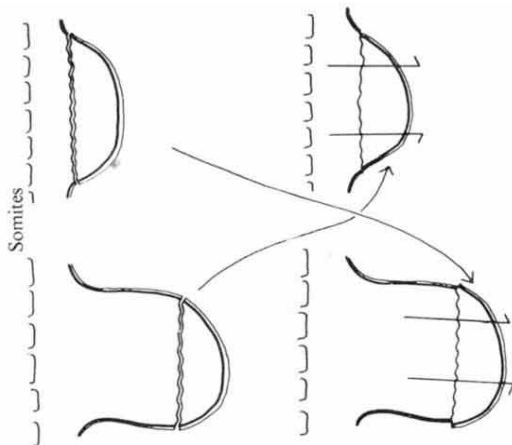
There is evidence that the course of the change in proximo-distal positional value which occurs in the progress zone is governed by its internal autonomous kinetics rather than by a level-specific signal from outside, for example from the apical ectoderm or the stump. The elegant and crucial work of Rubin and Saunders¹⁴ has shown that the influence of the apical ridge does not determine the axial level of the underlying mesenchyme. They showed that ectodermal caps can be exchanged between limb buds of different ages, each then developing into a normal limb. In terms of our model, the apical ectodermal ridge is needed to keep the mesenchyme labile at the tip, but it does not direct the path of progress there. The ridge issues a general permit rather than specific instructions.

From experiments in which the tips of two limb buds of different ages are exchanged (Fig. 4a) specification within the progress zone by a signal from the proximal stump can be ruled out. If both pieces of each composite bud develop according to their original presumptive fates, some parts of the resulting limbs will be missing or duplicated. If the stumps signal positional values to the tips, however, the presumptive fates of the tips will be radically modified. Our results, which will be reported in detail elsewhere, show that at least when the grafted tip is more than about $300 \mu\text{m}$ wide (that is, $300 \mu\text{m}$ from cut surface to apical ridge), the presumptive fate of the tip is not altered except perhaps in the immediate vicinity of the junction. Deficiencies and reduplications are regularly produced, and the measured size and form of the grafted distal regions resemble those of the donor control limb (Figs 4a–c and 5). These findings clearly exclude long-range signals controlling either growth or pattern formation in the distal region, and in particular rule out humoral mechanisms and mechanisms whereby elements already formed inhibit formation of further similar elements¹⁵. Similar results have been recorded by Amprino *et al.*¹⁶, but Hampé¹⁷ and Kieny^{18,19} have emphasized the regulative capacity of the chick limb bud, and have reported that grafted distal tissue may sometimes be converted to a more proximal character by the influence of proximal host tissue. Their evidence, however, is not compelling, and is not corroborated by further experiments of our own (D. S. and J. H. L., unpublished). The regulation they observe occurs chiefly in grafts of apical slivers so thin that the progress zone due to the apical ridge of the graft can extend into the host, and there bring about considerable regeneration of excised parts without any signalling of positional value. We do not rule out the possibility of some short-range interaction, however, by which cells co-operate to adopt a locally uniform, compromise character. Such a local smoothing interaction may well occur at the time of differentiation, outside the progress zone, and over short distances affect the histological interpretation of positional value. It could also occur earlier, inside the progress zone, and directly affect the assignment of positional value. We do not know how far the autonomy seen on a coarse scale corresponds to autonomy of individual cells.

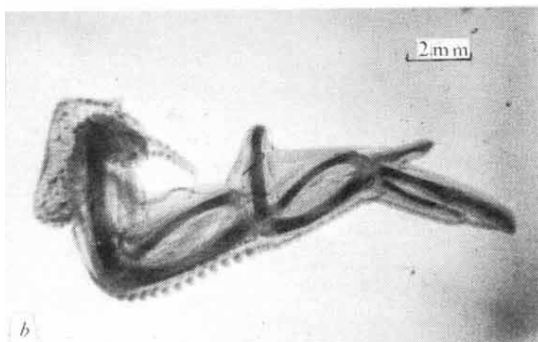
Application to Other Systems

The idea that positional information might be specified in growing fields by a timing mechanism, such as the counting of cell divisions in a labile zone, seems applicable to a variety of other systems. It could, for example, explain how positional values are assigned within a blastema so

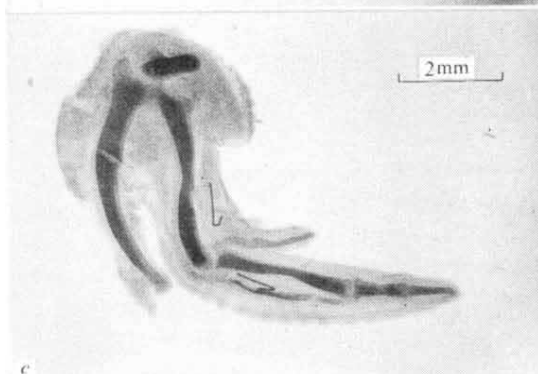
as to follow the rule of distal transformation². If blastema formation involves setting up a progress zone from the cells at the cut surface, then the regenerate will automatically originate at the positional value corresponding to the level of the cut, and from there develop only the more distal levels. Thus, for example, a blastema on the proximal face of the distal half of an amputated structure will yield a mirror image regenerate. This phenomenon occurs in the regeneration of both amphibian limbs²⁰ and insect imaginal disks²¹. A timing mechanism may also specify positional values in the retina, where they may be used for making the regular pattern of retino-tectal connexions²². Up to the stage when the system has its polarity specified, there is uniform cell division²³, but after this, growth is confined to a relatively narrow ring near the outer edge²⁴. Thus cells at the outer



a



b



c

Fig. 4 a-c, The whole of a stage 19 wing bud is exchanged with the distal quarter of a stage 24 wing bud (a, dorsal view). The grafts are held in place with pins. The outcome corresponds with negligible regulation. Typically a young bud on an old stump (b) gives a humerus and forearm of the same length as in the host's contralateral control wing, followed by a humerus, forearm and hand of the same length as in the donor's control wing. By contrast, an old tip on a young stump (c) gives a humerus of the same size as in the host's control wing, followed by a hand of the same size as in the donor's control wing. (The photographs in fact show composite limbs from two different pairs of chicks.)

Donor	Host				
Stage 19/20	20	22	24	24	24
Predicted composite limb					
Observed composite limb					
No. of cases	3	5	8	3	2

Fig. 5 An entire young wing bud is grafted on an older host stump, as in Fig. 4a. The stages of donor and host are as marked on the sketches in the top line. The predicted outcome is derived from fate maps²⁸ assuming no interaction between host and donor. The observed outcome is a mean, derived from measurements on several composite limbs; the number of measured limbs is shown in the bottom line. Apart from some possible local regulation affecting not more than about half an element, the observations agree with the predictions.

edge of the mature retina have divided more times than those nearer the centre. There may thus be a progress zone during retinal growth which could provide the retinal cells with a radial coordinate analogous to the proximo-distal coordinate in the limb.

Specification of Positional Value

We have proposed a new mechanism, based on autonomous changes of positional value with time rather than on signals from far off, to specify positional information in a growing system. On this basis, a model can be developed to give quantitative predictions of the outcome of various grafts; and these predictions are consistent with the experimental data (D. S. and J. H. L., unpublished). Several questions now require further investigation. For example, how is positional value registered by individual cells and is it a continuous variable? Does it change only at cell division, suggesting an analogy with regulation in the insect epidermis³ and with Holtzer's "quantal mitosis"²⁵? Are individual cells autonomous, or is there local averaging of positional value by short-range communication between cells inside or outside the progress zone? How does the apical ectodermal ridge specify the width of the progress zone; is hyaluronic acid involved, as some recent experiments²⁶ perhaps suggest?

More generally one can begin to see how positional information may be specified in different systems, using, in different ways, three principal components: a positional value, a positional signal, and cell division. In *Hydra* a new boundary region may be formed when the signal is a threshold amount below the positional value; in the insect epidermis the positional signal sets the positional value at cell division; in the vertebrate limb bud the positional value changes autonomously at cell division; and in intercalary regeneration in the insect limb differences between the signal and the intrinsic value may initiate cell division²⁷. Our analysis of the chick limb strongly indicates that one should look for a biochemical correlate to the proposed changes in positional value in the progress zone. While suggesting where to look, and what to look for, it unfortunately provides no indication whatsoever as to how to do it.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Distance Measurements across the Heimaey Eruptive Fissure

IN describing the latest Icelandic eruption, Kirkjufell, Thórarinnson *et al.*¹ showed how it began as an erupting fissure about 1,600 m long and how activity ceased on all but the central three vents after 3 d. We have made precise distance measurements between four fixed stations located around the southern end of the fissure (Fig. 1) on two visits in February and April. The measurements, made with the National Physical Laboratory Mekometer III prototype^{2,3}, corrected for atmospheric refractive index and modulating frequency, are shown plotted with their expected errors against time in days after January 23 on Fig. 3. Also shown on Fig. 3 are the curves of the form

$$d = d_0(1 - \exp(aT))$$

where d is the strain at time T , d_0 is the strain at time zero and a is the inverse of a time constant, which best fit the observed results. Each best fit has the same time constant, 7.5 d, and is in good agreement with the observations, excepting the April result of line 3-1A.

We have thus assumed that the observed strains result from a single system which relaxed exponentially after the start of the eruption with a time constant of 7.5 d. The relaxation continued in this way for the two lines perpendicular to the fissure at least until early April, although some other process governed the changes on the longitudinal line, 3-1A, after February.

We calculated the asymptotes and lengths at time zero, and thus the recoverable strain at the time the eruption started, for each line. There is presumably also a non-recoverable component of unknown magnitude associated with the crustal spreading, so that our strain values must be minima. They are: on line 1-2, 340 p.p.m.; on line 3-4, -74 p.p.m.; on line 3-1A, -409 p.p.m.

Ramsay⁴ shows that the strain E in a direction θ to an orthogonal set of an extension E_1 and a compression E_2 is given by

$$E = \frac{1}{2}(E_1 + E_2) + \frac{1}{2}(E_1 - E_2)\cos 2\theta$$

Using our calculated values of the original strains on the three lines, we found that $E_1 = 36$ p.p.m. and $E_2 = -420$ p.p.m., and that the axis of maximum compression is orientated at

N 45° 21' E. This is very nearly a state of pure shear; indeed the deviation of this result from pure shear may represent the crustal displacement produced by the eruption.

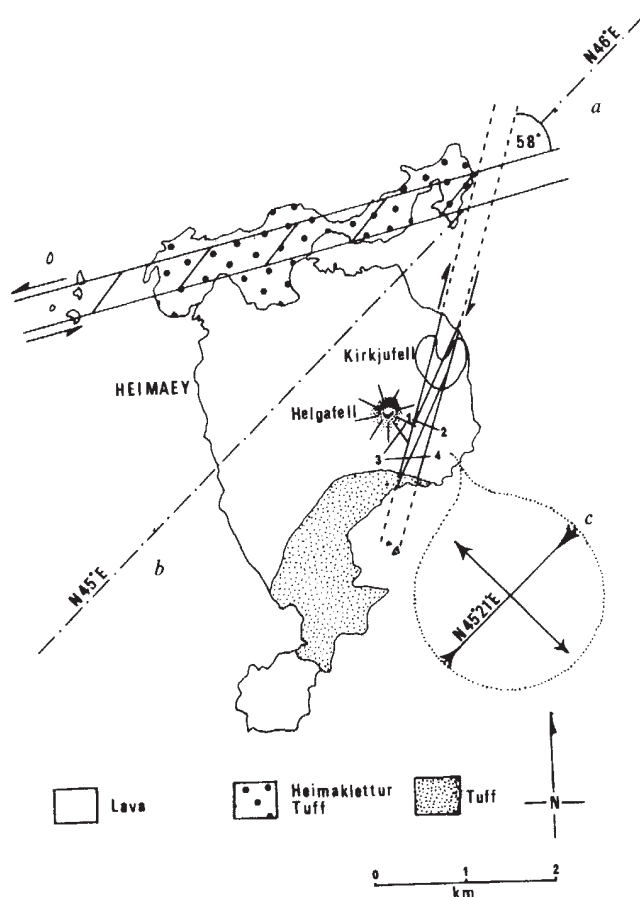


Fig. 1 Geological map of Heimaey showing the relationship between the distance measurements and the inferred shear zones. *a*, Direction of maximum compression to produce conjugate shear zones; *b*, regional trend of the active zone in south-central Iceland; *c*, maximum compression (Mekometer results). 1-2, Mekometer line.

Most observers¹ of the early activity along the whole length of the fissure consider that the active vents were in a straight line trending N 17° E, but our mapping by compass indicates that there are at least two sections of the fissure arranged *en echelon*. The eight most southerly vents line up along N 24° E, and the line of the three vents still active in February has a N 27° E trend; this suggests a zone of right-lateral shear.

Jakobsson⁵ regards the Heimaklettur formation, the oldest on the island, as a fissure eruption, possibly subglacial, trending N 75° E, but composed of five *en echelon* units whose individual strikes are about N 35° E; this suggests a zone of left-lateral shear, the strike of which differs from that of the present eruption by 58° (Fig. 1).

Similarly, Thórarinnsson⁶ described the submarine activity during the Surtsey eruption as being on a system of fissures with trends of about N 35° E covering a zone 5 km long and striking at N 65° E; as in the case of Heimaklettur, this suggests a zone of left-lateral shear.

Assuming these three inferred shear planes to belong to the same conjugate set, the axis of maximum compression should lie in the plane bisecting the angle between the left and right-lateral members, N 46° E (Fig. 1), almost the same as both the compressive direction deduced from the original strains calculated from the Mekometer results and the direction of the volcanic and tectonic features in the south-central active zone in Iceland.

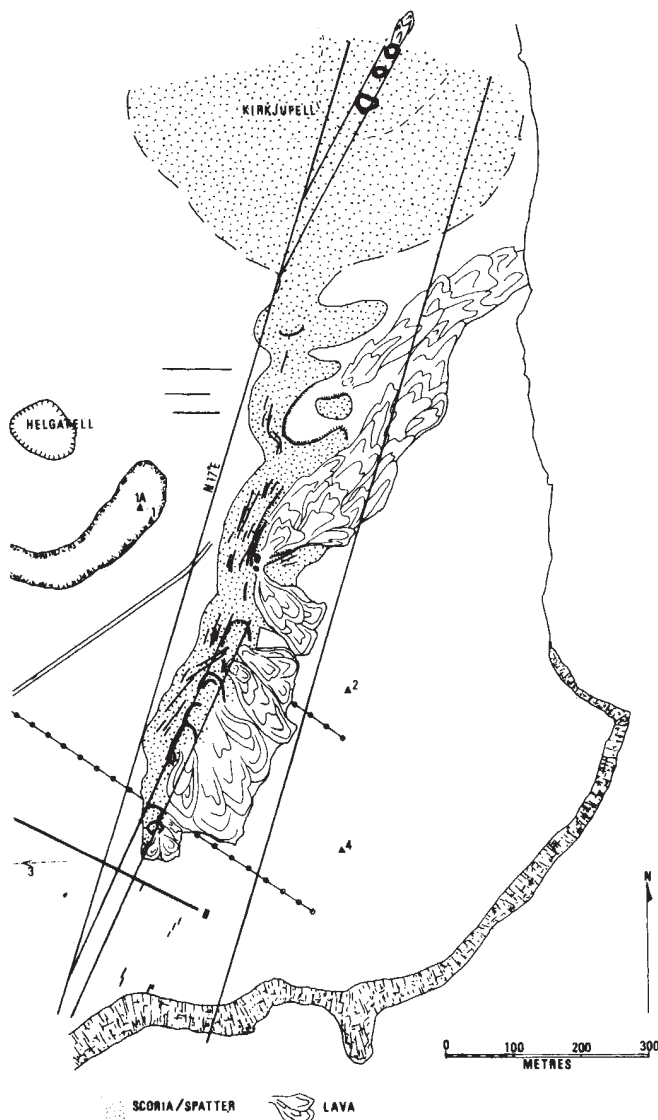


Fig. 2 Geological map of the southern part of the active fissure (February 7). ▲, Mekometer station; /, fissure.

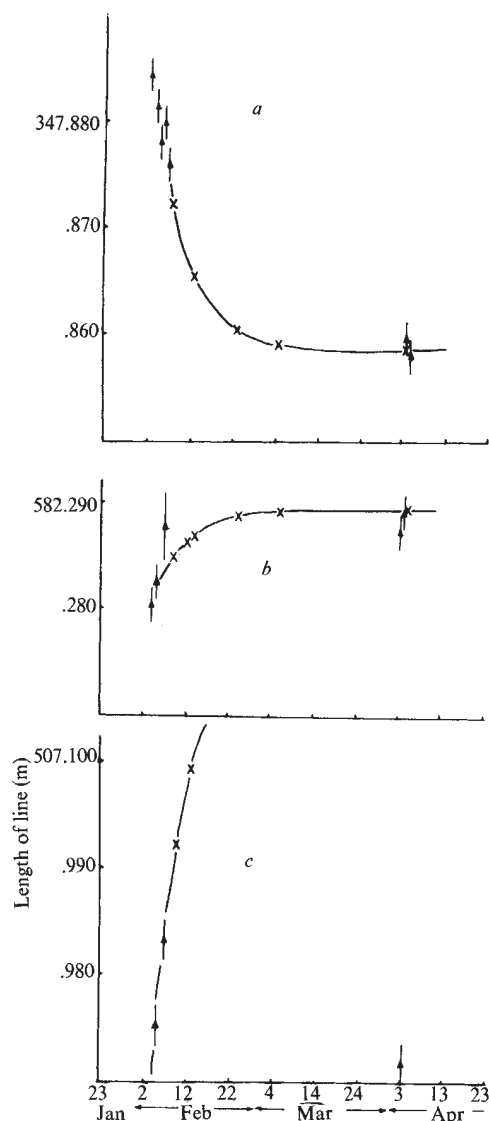


Fig. 3 Changes in length of the three measured lines from February to April. ▲, Mekometer measurement with standard deviation; x, theoretical exponential relaxation of strain. a, Line 1-2; b, line 3-4; c, line 3-1A.

There are two important conclusions to be drawn from these results. First, they show that not all eruptions show the radially symmetric strain pattern of detumescence proposed by Mogi⁷ and found in the eruptions of Kilauea⁸. The difference presumably lies in the linearity of this eruption, and it might even be that all linear eruptions result from applied shear stresses. Second, the inferred stress system agrees very well with the proposed spreading axis through the south-central active zone in Iceland, as it shows a minimum compression acting at N 44° W, almost exactly the expected spreading direction. Heimaey lies at the extreme southern end of this zone, which may explain why the normal faulting associated, from seismological evidence⁹, with spreading ridges, and indeed found further north, has given way to the observed shear tectonics.

We consider that such a change in the tectonic response along the axis could come about through a relative southward decrease of the least compressive stress. The petrochemistry of the basalts from this spreading axis shows a gradual change southward also, with tholeiites predominant further north, transitional basalts in the Hekla-Katla region and alkali-olivine basalts in the Vestmannaeyjar¹⁰.

This decrease of the least compression towards the end of the spreading axis we consider to lend support to Piper's model¹¹

and that it is therefore unnecessary to invoke a transform fracture zone in Southern Iceland in order to connect the Mid-Atlantic Ridge to the south-central active zone.

We thank Dr G. P. L. Walker for suggestions; the Icelandic authorities, especially Professors Thórbjörn Sigurgeirsson and Sigurður Thórarinnsson, for help; Dr K. D. Froome, Mr R. H. Bradsell and the Director of the National Physical Laboratory for making the prototype Mekometer available; and the Royal Society for financial support.

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Earth Tidal Amplitude and Phase

DURING the summer and autumn of 1970 a NASA Goddard Space Flight Center laser tracking system tracked the Beacon Explorer C spacecraft from the Goddard Optical Facility in Greenbelt, Maryland. The tracking system provided distance measurements to the satellite at a rate of one per second with a precision of 30 to 50 cm on as many as four consecutive passes each day, weather permitting. The satellite, Beacon Explorer C, carries laser retro-reflectors and is in a near circular orbit at an altitude of about 1,000 km with an inclination to the equator of 41°.

The laser range measurements to the satellite from this single tracking station have been used to determine its orbit for nearly five months in 1970 and, because the latitude of the tracking station is similar to the orbital inclination, the inclination is the best determined parameter. It is the inclination that we discuss here. The original purpose of this investigation was to try and observe the change in latitude of the tracking station arising from polar motion¹ but in the course of the analysis the perturbation of the inclination by the Earth and ocean tides had to be accounted for.

From a point in space, the basic tidal response of the Earth to the gravitational attraction of the Moon appears as a small elongation of the Earth's shape (bulge) in the general Earth-Moon line. A similar elongation, or distortion, is caused by and directed roughly towards the Sun. To an observer on a satellite, the tides appear as a distortion of the gravitational field arising from the tidal bulge which is associated with the motions of the Sun and Moon rather than the rotation of the Earth. Thus, the perturbations of a satellite orbit arising from the tides are primarily determined by the motion of the satellite and its orbit with respect to the Moon and Sun rather than with the motion of the Earth. Hence, to a satellite there are no significant perturbations associated with the large semi-diurnal and diurnal tides that are observed on the Earth but only with the tidal (and other) terms of longer period, such as a few weeks to years. For the Beacon Explorer C satellite the largest terms in

the perturbation of the inclination have periods of 85 d, one coming from the Sun and the other from the Moon, and amount to the time required for the orbital plane of BE-C to rotate once (about 4.25° d⁻¹) with respect to the First Point of Aries and the node of the Moon's orbit. The other major terms have periods of 34 d and 10 d, corresponding to half the rotation period of the orbital plane with respect to the Sun and Moon respectively.

For a solid Earth the magnitude of the tidal perturbations of the orbit would be directly proportional to the magnitude of the physical distortion of the surface by the tides, representable in magnitude by Love's number k , which is the ratio of the tidal potential to the tide rising potential. But for the real Earth, the magnitudes of the perturbing forces are probably modified by the additional influences of the oceans and the true nature of these forces as they affect a satellite are not presently fully understood.

The orbital inclination of Beacon Explorer C has been determined on twenty-eight occasions in a period of nearly five months. Only laser range measurements from the Goddard tracking station were used in the analysis and each determination of the orbital inclination was obtained from data collected on four consecutive passes of the satellite, spanning a period of 6 h. The values of the inclination over the five month period showed considerable variation (about 20 arc s), as we expected, but after subtracting the perturbations caused by the Earth's gravity field, the Sun and Moon's gravity and solar radiation pressure, and allowing for the change in latitude of the station arising from polar motion, a variation of 2 arc s still remained. This remaining variation had a very distinctive structure which can be almost entirely explained as Earth tidal perturbations.

We have calculated the effect of the Earth tides on the orbit numerically from the simplest of tide potential models, that is, a second degree spherical harmonic expansion about an axis offset slightly from the direction of the tide rising body to allow for a phase lag in the tidal response of the Earth. In this representation no differentiation has been made between the continental crust and the oceans. The effect of both the solar and lunar Earth tides has been included in the orbital computations with the restriction that the Love number, k_2 , and the phase, ϕ_2 , are the same for both the lunar and solar tides.

The theoretical perturbation has been compared with the observed inclination residuals for several values of k_2 and ϕ_2 . The initial comparisons were made with $\phi_2=0$ from which it soon became apparent that k_2 was around 0.25. Prior to this analysis we had anticipated that k_2 would be in the range 0.29 to 0.31 because these are the values that are being obtained from surface measurements, such as horizontal pendulums² and seismicity³. For all values of k_2 near 0.25 the differences between the observed and computed values of the inclination showed systematic variation and it became necessary to introduce a phase lag (ϕ_2) into the perturbations. After several tests the values of

$$k_2 = 0.245 \pm 0.005 \text{ and } \phi_2 = 3.2 \pm 0.5^\circ$$

were obtained as the best values where the fit to the data was 0.045 arc s standard deviation. The essential effect of introducing the phase was to reduce the standard deviation of fit to the data by about 35%. Neglecting the phase altogether led to the same optimum value of k_2 but with a larger standard error. In Fig. 1 we show the residuals to the inclination (after all but the Earth tides have been removed) and the theoretical tidal perturbation for the optimum values of k_2 and ϕ_2 . The agreement between the laser data and theory is evident.

The gravitational field model used in this analysis was GEM 1 (ref. 4) with modified values for the 19th degree and the 13th order terms with which the BE-C satellite is resonant. GEM 1 is a field complete to degree and order 12 with selected higher resonance terms and zonals out to degree 21. When the original GEM 1 (19,13) resonant terms were used in this analysis the residuals about the tidal curve showed a periodic structure of 0.063 arc s and period 5.5 d. This pattern was used to derive

new values of the 19th degree and 13th order terms and the data were then reanalysed. The adjustment to the (19,13) terms amounted to approximately 15% in the cosine term and 20% in the sine term. It is with the GEM 1 gravity field containing these two modified coefficients that the present results have been obtained.

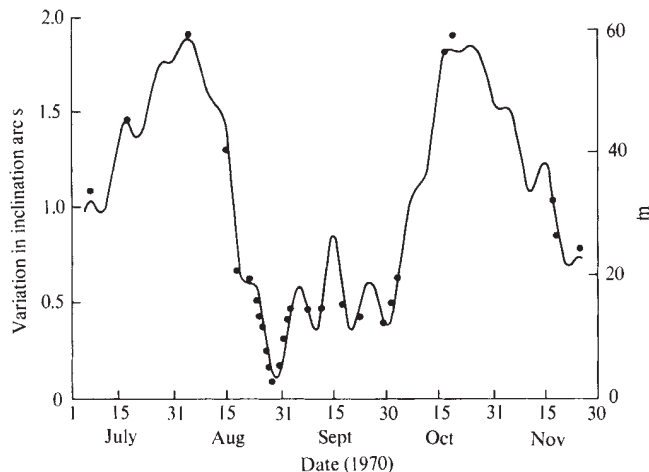


Fig. 1 The perturbation of the orbital inclination of the Beacon Explorer C spacecraft arising from the Earth and ocean tides. The dots are values of the orbital inclination derived from laser range measurements. The continuous line shows the theoretical perturbation computed from a second degree spherical harmonic representation of the solar and lunar tides with Love's number $k_2=0.245$ and a phase lag of 3.2° . The right hand vertical axis shows the variation in inclination projected onto the Earth's surface. The r.m.s. deviation of the observed points to the theoretical curve is 0.045 arc s (1.38 m).

The amplitude of the observed perturbation of the orbit is smaller than expected if the true value of Love's number, k_2 , for the Earth is around 0.3, as is generally accepted. The simple model of the Earth tides upon which the theoretical curve was based must thus be inadequate. But the detailed agreement between the observed points and the theory necessitates the form of the perturbation for the BE-C satellite to be a second degree spherical harmonic. Thus, the perturbing influence that is modifying the computed tidal variation can only have a cancelling effect and in no way modify the form of the disturbing function for the satellite. W. H. Munk (personal communication) has indicated that this effect can probably be attributed to the ocean tides, and recent work by Lambeck and Cazenave⁵ corroborates this view. Lambeck and Cazenave suggest that certain terms in the tidal potential function of the oceans cause perturbations of the orbit almost identical in form to the solid Earth tide. But the magnitudes of these ocean perturbations have a different variation with orbital parameters than the solid Earth perturbations. Thus, they suggest the observed tidal perturbations will depend on the orbit of the satellite being studied, and the determinations of k_2 (from satellites) so far⁶⁻⁸ strongly support this viewpoint. Thus, orbital perturbation techniques may soon be in a position to provide quantitative information on certain components of the ocean tides.

The analysis reported here is probably the most precise determination to date of the amplitude and phase lag of the Earth and ocean tides from the tidal perturbations of a satellite. The use of high precision laser range measurements (30 to 50 cm) at a high repetition rate (1 s^{-1}) permitted the computation of very short orbital arcs of 6 h duration. This short averaging time permitted some of the fine structure of the perturbation to be revealed. The good agreement between observation and theory clearly shows that the tidal disturbing potential (for the Beacon Explorer C satellite) can be almost entirely represented

by two second degree spherical harmonics offset by a few degrees from the directions of the Sun and Moon.

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Mesozoic Palaeomagnetic Scale of the USSR

WORLD data on palaeomagnetic Mesozoic stratigraphy have been summarized by several people¹⁻³. The integrated palaeomagnetic reversal columns they obtained differ from one another partly because they have been drawn up from different data and partly because of small differences in the criteria used to define the fundamental palaeomagnetic stratigraphical units—palaeomagnetic zones. Here we give regional palaeomagnetic columns (Fig. 1) obtained recently as a result of detailed palaeomagnetic investigations of Mesozoic sedimentary formations of the USSR.

In order to coordinate the palaeostratigraphical data we used available USSR palaeomagnetic data²⁻¹⁶ and the 1964 geochronological scale¹⁷ of the USSR. Some errors caused by a lack of correlation between local stratigraphical scales and the integrated geochronological scale, the latter not being perfect itself, are inevitable. If radiometric determination of a stage boundary age has not been made and if only data concerning the boundaries between sections or systems are available, the time interval is divided into equal parts within the stage quantity (such boundaries are shown as diagonal lines in Fig. 1). At some parts of the section we assumed constant deposition rates; thus we managed to translate from sections and beds to the time scale. This made it possible to estimate roughly the duration of palaeomagnetic zones. The geological time scale was divided in palaeomagnetic intervals and zones. These intervals and reversed (R) zones have been given local geographical names.

We note that palaeomagnetic—stratigraphic comparisons in the USSR are based almost exclusively on palaeontological data. Unfortunately good stratigraphic sections are not usually satisfactory for palaeomagnetic investigations; on the contrary, those favourable for defining palaeomagnetic research sections do not have fossils. This makes it difficult to correlate regional palaeomagnetic columns, in order to estimate accurately the length of R zones and to draw up an integrated palaeomagnetic time scale. For example, the R zones in Santon and Campan are likely to be the same as the Kuldijian zone, because in each section we see only one zone in this time interval. The same may be true for Gatan, Chagyl and elsewhere. In Central Asian sections, correlation is difficult because of scarcity or absence of fauna.

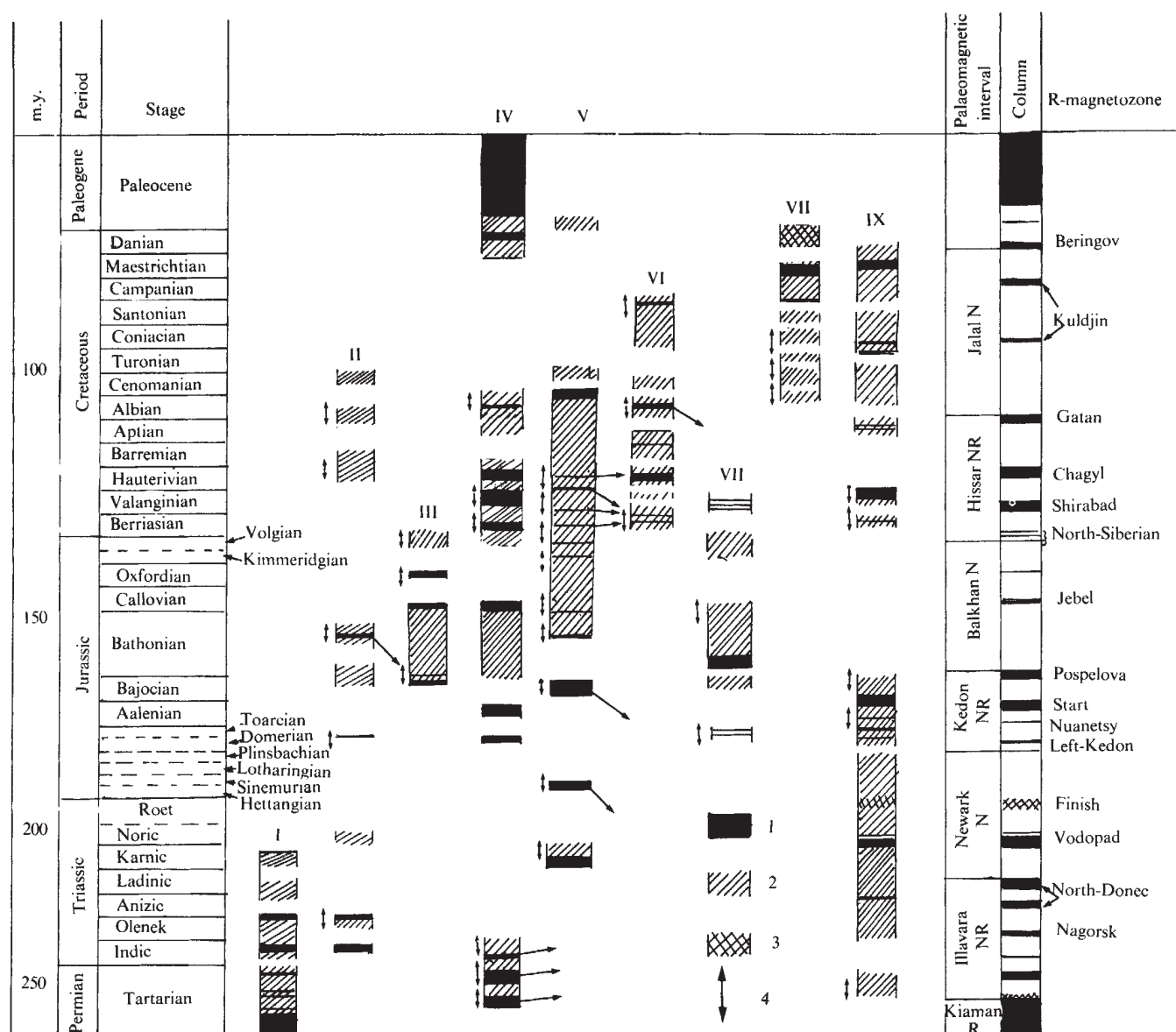


Fig. 1 Correlation of regional palaeomagnetic Mesozoic scale of the USSR. I, Russian Platform^{5,6,8,10}; II, Donbas and Crimea^{4,8,13,16}; III, Azerbaidjan³; IV, Turkmenistan and Western Kazakhstan^{8,11,13,15}; V, Tadjikistan, Tadjik Depression^{3,6}; VI, Fergana^{3,9,14}; VII, north Siberia^{3,12}; VIII, Sakhalin³; IX, north-east Asia^{2,3}; X, palaeomagnetic Mesozoic scale of the USSR. 1, Palaeomagnetic R zones; 2, N zones; 3, zones of mixed polarity; 4, approximate position of boundaries or duration of palaeomagnetic zone.

An analysis of the integrated Mesozoic palaeomagnetic column shows, first, that in Mesozoic sediments, natural remanent magnetization of normal polarity prevails; corresponding to more than 80% of the time in the Mesozoic era, the geomagnetic field had normal polarity.

Second, there may be as many as twenty palaeomagnetic R zones; their duration runs from 0.5 to 3 or 4 m.y. with an average of about 1.5 m.y. The duration of N zones runs from 0.5 to 20 m.y.

Third, distribution of R zones in time is not even; there is a tendency for interchanging "thicks" and "thins" of geomagnetic field reversals. The intervals last 20–40 m.y. Beginning with the middle of the Tartarian stage of late Permian (after the Kiaman R interval) and finishing in the Palaeocene, seven palaeomagnetic intervals were obtained (Fig. 1). Two intervals—Illavara and Jalal—are the most reliable.

Our suggested scheme is not complete. It is possible that new R zones will be discovered and that some uncorrelated zones will be liquidated before an exact column is determined, but we believe that the overall picture of the distribution and total duration of palaeomagnetic intervals and zones will not change.

We have summed up the initial stage of accumulating palaeomagnetic data for the Mesozoic in the USSR. In order to draw up the world palaeomagnetic scale for Mesozoic and other eras it is necessary: that detailed palaeomagnetic investigations be made using all available modern methods of the most complete and uninterrupted sedimentary and volcanogenic sequences in a number of world regions to draw up palaeomagnetic stratotypes; that stratotypical sections be dated by different methods (radiological, palaeontological); and that a nomenclature of palaeomagnetic stratigraphy be worked out.

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Ancient Metamorphic-migmatite Belts of the Brazilian African Coasts

ABOUT 150 m.y. ago, a successful rift formed which led to the separation of present day South America from Africa. Many types of rocks from Precambrian migmatites to Lower Cretaceous evaporites¹ match across the junction of rifting; but why do continental masses rift where they do? The answer could lie in purely random phenomena, but time after time ancient trends and structures seem to control later events. If events in the mantle are random, perhaps they lead to successful amplification only when they interact with certain structural situations in the continental crust. Only recently have sufficient data become available on the basement rocks of the Atlantic coasts of Africa and Brazil to allow a preliminary synthesis. But it seems certain that the rifting followed an ancient intercratonic structural trend (mobile belt) with a complex history of metamorphism and magmatism. The rifting process was not random.

The general structure of the two continents (Fig. 1) is well known^{2,3}. Stable continental nuclei with ages in the 3,000 m.y. range are surrounded by younger metamorphic belts. The older belts tend to be in the granulite facies of metamorphism and are associated with charnockites and migmatites. Metamorphism in these is of the Abukuma type and their mineralogy suggests thermal gradients of the order of $60^{\circ}\text{C km}^{-1}$ or more. These ancient metamorphic belts are followed by many younger belts with typical Barrovian facies series indicating lower thermal gradients. In fact, the trends could be correlated with a general decrease of thermal gradients with time of magnitude $0.03^{\circ}\text{C/m.y.}$ Along the Atlantic coasts of South America and Africa there is widespread development of ancient high temperature/low pressure metamorphic rocks and it is along this belt that parting occurred.

Experimental studies of granite production^{4,5} indicate that the granulite-charnockite-migmatite association represents a situation at the base of the acidic crust where partial melting occurs. Such ancient basement crust has been uplifted to form the zone of continental splitting. It seems reasonable that the large heat fluxes needed for migmatization may be associated with the rise of basaltic magma from the upper mantle. Thus

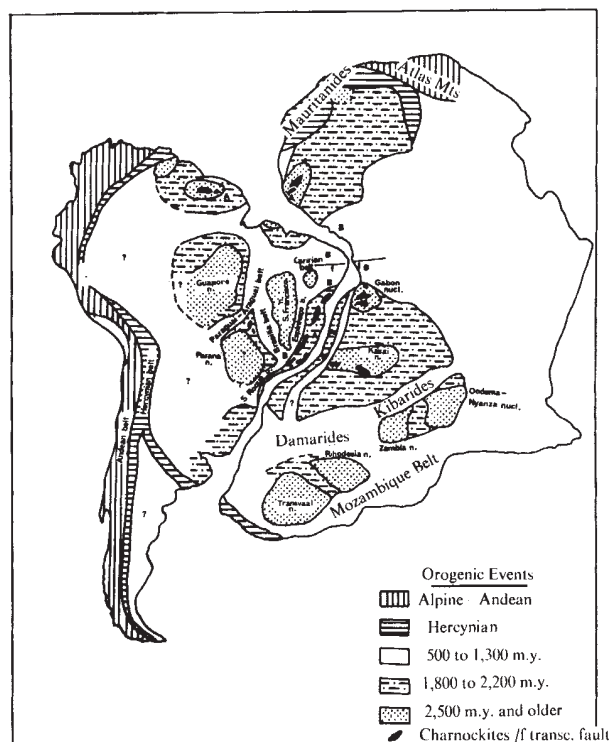


Fig. 1 Tectonic regions of Africa² and Brazil³. H, High pressure; B, intermediate pressure (Borrovian); A, low pressure (Abukuma).

in forming the high grade assemblages one may expect a series of steps such as the following.

- (1) The creation of a thermal anomaly in the upper mantle (plume) which leads to surface basalt eruption and general heating of the crustal region.
- (2) The fusion of the base of the crust and the start of acid plutonism and volcanism.
- (3) Once the base of the crust becomes "sticky" on a large scale, basalt cannot be extruded but instead it flows beneath the low viscosity crust. This basalt may differentiate to produce peridotite-anorthosite complexes because of the very long cooling time in a hot environment. Basalt injected at even greater depth could crystallize to eclogitic complexes. We thus expect the observed association of basaltic differentiates and anorthosites with the migmatite-charnockite regions.

The arguments presented below indicate that separation along a zone of uplifted granulitic basement may not be accidental. We imagine that mantle thermal anomalies (plumes) can arrive under any crustal section by random processes. If a plume arrives beneath a cratonic region with a thick granitic layer we might expect a series of events as follows.

- (a) Dyking of the crust (some spreading and uplift) and surface eruption of basalt.
- (b) Gradually the base of the crust is heated and partial melting commences.
- (c) Granitic plutonism and acid volcanism commences. When the base of the crust has a large melt fraction and hence a low viscosity, basalt penetration ceases.
- (d) Basalt from the upper mantle is injected beneath the crust. At high levels it differentiates perfectly (possibly with extensive contamination) to produce rocks of the anorthosite-peridotite suite. At lower levels eclogite forms.
- (e) Extensive development of eclogite loads the overall active zone and downwarps the upper mantle melting zone.

- (f) Plumes migrate laterally and the craton is preserved but thickened at the base with basaltic material. It is for this reason that ancient cratons tolerate successions of basaltic invasions but still survive. The plumes are transient.

If a similar plume arises under a mobile belt where granulitic basal crust underplated by basalt is uplifted, flood basalts and dyking will occur. There is insufficient high level granitic phase to cut off basalt extrusion. A successful spreading ridge results and the continent splits. We consider that such models may explain why old mobile belts become the sites for future continental fission and that the type of high grade metamorphic rocks on the Atlantic margins of South America and Africa is not accidental. Under zones of thick granitic crust, plumes may be transient and will persist only under regions of thin acid crust, an ocean ridge type situation where most basaltic magma is injected near the surface.

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High Resolution Map of NGC1265

THE radio sources associated with NGC1265 and IC310 have "head-tail" structures with the heads coinciding with the optical galaxies¹. Ryle and Windram suggested¹ that both radio sources were ignited by a relativistic particle wind from the nearby Seyfert galaxy NGC1275. Hill and Longair² drew attention to further examples of galaxies in clusters with the same peculiar radio morphology.

This "interacting galaxies" hypothesis has been criticized³, and it has been suggested that galaxies such as NGC1265 are radio sources in their own right, not causally connected with any other galaxy. The elongated radio tails are then explained as trails left as active radio galaxies plough through the cluster medium. Here we present a high resolution map of NGC1265 which provides further evidence in favour of the "radio trail" hypothesis and thereby argues for the existence of an intra-cluster medium.

The observations were made with the Westerbork synthesis radio telescope at 5 GHz during 4 sets of 12 h in December 1972 and January 1973. Interferometer baselines ranging in length from 36 m to 1,458 m in steps of 18 m were used. Our resulting map has an elliptical synthesized beam 6×10 arc s to half power, with a first diffraction grating ring whose size is 11×17 arc min. The system temperature was 200 K and the bandwidth 4 MHz, giving an r.m.s. noise on the map equivalent to 0.6×10^{-29} W m⁻² Hz⁻¹ per synthesized beam.

In Fig. 1 we show the new 5 GHz map superimposed on the blue Sky Survey print. A diffraction grating ring due to the nearby strong radio galaxy NGC1275 confused part of our original map, but the influence of this source has been removed using a point source subtraction program. For comparison, the lower resolution 1.4 GHz map of NGC1265 is given in Fig. 2, also superimposed on the optical photograph. In both cases only the most intense region of the source near the optical

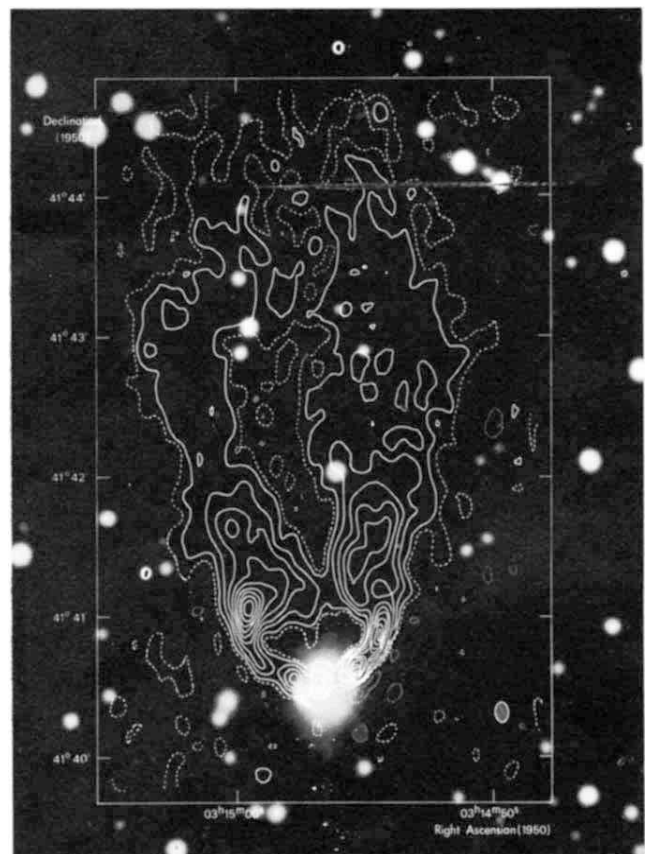


Fig. 1 Westerbork 5 GHz map of NGC1265 superimposed on the blue Palomar Sky Survey print. Continuous contours are plotted at intervals of 2.5 m.f.u. per synthesized beam from 2.5 m.f.u. to 22.5 m.f.u. Dashed and dotted contours indicate the 1.25 m.f.u. and -1.25 m.f.u. levels respectively. No correction is made for the effect of the 10 arc min primary beam centred at RA 03 h 15 min, dec. 41° 45'. The shaded ellipse corresponds to the half-power synthesized beam.

galaxy is shown because the fainter part of the tail is mostly below the noise level at the full resolution of the 5 GHz system.

The superpositions, accurate to ~ 2 arc s near the nucleus of NGC1265, were carried out using optical positions of two nearby stars supplied by Mme Heidmann. Bertola and Perola⁴ have found optical emission out to 100 arc s from the nucleus so the optical image of the galaxy covers a large part of the 5 GHz map.

There are several striking characteristics of the map: the semicircular shape of the radio head; the discrete components within that semicircle; the prominent central component near the nucleus of the galaxy; the deep well behind the head; the two ridges of emission behind the well which stretch far down the tail; the central connexion behind the well which forms a bridge between these two ridges; and the general symmetry of the source.

It is difficult to envisage how such a radio source could be ignited from NGC1275 or any other galaxy; we shall interpret these features only in terms of the "radio trail" hypothesis. The simplest version of this hypothesis⁵ is shown schematically in Fig. 3 with the 5 GHz contour diagram. Here NGC1265 is assumed to be travelling with a transverse velocity v_e in the direction indicated, recurrently ejecting pairs of radio-emitting blobs with transverse velocity v_e into the intergalactic medium.

The shape of the head and the width of the tail are determined by the ratio v_e/v_g , by the angle between v_e and v_g and by the deceleration of the components. The latter depends on the component masses and cross sections and on the density of the intergalactic gas. A line joining components A₁ and A₂ (Fig. 3) would be almost perpendicular to the symmetry axis of the source, implying that v_e and v_g are oriented approximately

at right angles. (This is probably fortuitous because other head-tail sources such as 3C129 and IC310 show no evidence for the same alignment.) In this case a good fit to the shape is given by values of v_e/v_g ranging from 1 to 3. The predicted trajectory for $v_e/v_g=2$ is shown in Fig. 3. NGC1265 has a radial velocity of $\sim 2,300 \text{ km s}^{-1}$ with respect to the mean of the Perseus Cluster⁷ and we assume that the transverse velocity, v_g , is of that order. Our observations therefore imply injection speeds of a few thousand km s^{-1} , comparable with those now believed to occur in simple double radio galaxies⁸.

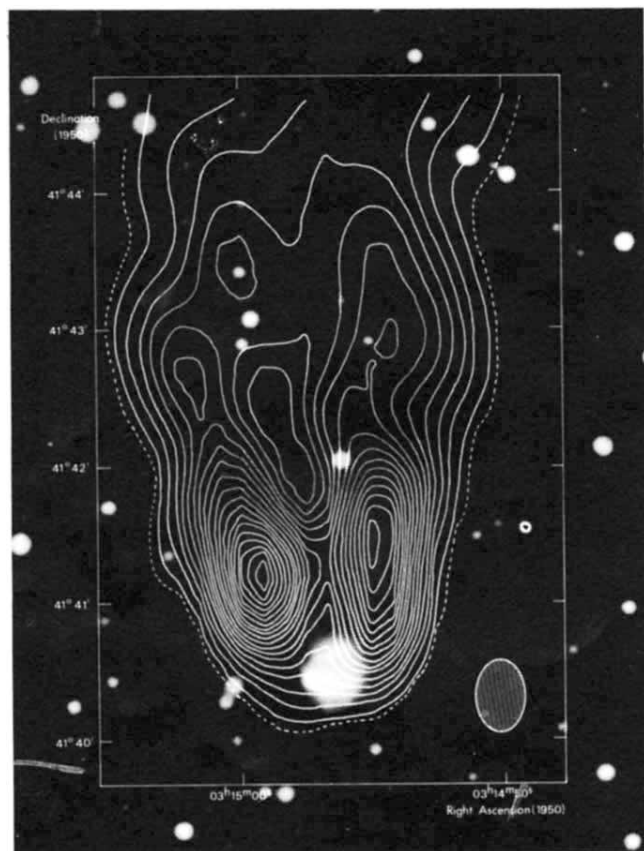


Fig. 2 Westerbork 1.4 GHz map of NGC1265 superimposed on the blue Palomar Sky Survey print. Continuous contours are plotted at intervals of 18.5 m.f.u. per synthesized beam from 18.5 m.f.u. to 351.5 m.f.u. Dashed contours indicate the 9.25 m.f.u. level. No correction is made for the effect of the 36 arc min primary beam centred at R.A. 03 h 15 min, dec. $41^\circ 38'$. The shaded ellipse corresponds to the half-power synthesized beam.

The discrete components in the radio emitting arc show that the ejection is repetitive. Assuming NGC1265 is at 60 Mpc and $v_g=2,000 \text{ km s}^{-1}$, $\sim 4 \times 10^6 \text{ yr}$ is the typical period between principal outbursts. Each of these requires a minimum energy of 10^{55} erg . The length of the tail at 1.4 GHz implies continual activity for at least 10^8 yr .

The front central component of Fig. 1 is absent from Fig. 2. It has a flux density of $(27 \pm 3) \times 10^{-29} \text{ W m}^{-2} \text{ Hz}$ and lies 4 arc s south-west of the optical centroid measured by Heidmann. Because this is within the errors of the optical measurement we presume that the component is associated with the nucleus of NGC1265. A comparison with the lower resolution Westerbork 1.4 GHz (Fig. 2) and Cambridge 2.7 GHz (ref. 9) maps shows that the nuclear component has a flatter spectrum than the source as a whole, indicating that it is partially opaque, compact and presumably active. The flat spectrum nuclear components in NGC1265 and 3C129 resemble those already known to occur commonly in classic double radio galaxies (such as 3C390.3, ref. 10, and 3C310, G. K. M., and

H. L., unpublished) and provide further evidence that similar activity is occurring here.

A possible faint emission ridge (T) stretches across the well towards the nuclear component. It is tempting to interpret this as a trail of the nucleus itself which is simmering between major eruptions reminiscent of the variable galactic source associated with Cyg X-3 (ref. 11).

The well enclosed by the radio head can be explained because the component pairs A_1A_2 and B_1B_2 are presumably young, still highly confined by the ram pressure of the medium, and have not begun to diffuse backwards along their trajectories. The more relaxed ridges of emission in the tail and the central connexion between them are formed by older components that have reached the expansion stage. The contour map is somewhat deceptive here because it suggests that the connexion occurs only just behind the well. But the bridge between the ridges may be present all along the tail because even if it continued at the same relative intensity it would fall below the noise level of the map.

The profiles C_1C and C_2C are very similar to intensity profiles along the major axes of many double radio galaxies. The steep outer and gentle inner gradients suggest that the components evolve in the same way as those in double sources. Initially they are confined by ram pressure, but soon the rear portions of the components expand back along their own trajectories, where they meet least resistance. This expansion may form a bridge, well known in double sources and present here behind the well. Ultimately the components are stopped and fade away as they expand against the static pressure of the medium. The contrast between the outer and inner gradients then slowly disappears. The detailed structure may then be dominated by the magnetic field of the galaxy as described in the magnetospheric model⁶.

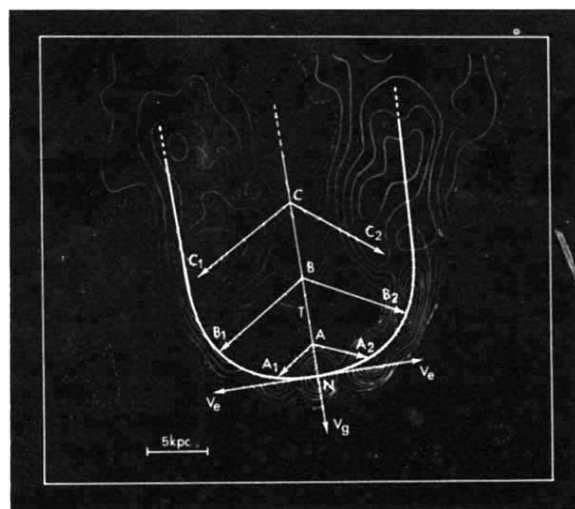


Fig. 3 Schematic diagram of a simple "radio trail" model superimposed on the 5 GHz contour map of NGC1265. The galaxy moves with transverse velocity v_g recurrently ejecting pairs of radio emitting blobs (A_1, A_2), (B_1, B_2), (C_1, C_2) with transverse velocity, v_e . We note the presence of a possible faint emission ridge T.

The source symmetry is also comparable to that apparent in many double radio sources. The flux density ratios for the different pairs are within a factor ~ 3 and the luminosity from one pair to the next does not differ greatly. In addition the width of the tail is quite constant throughout its length. Thus successive major events repeat at very similar power levels and ejection velocities. The phenomenon that we witness in NGC1265 is extremely informative because it spatially separates these different events in time. In the usual double radio galaxies, the effects of such repeated eruptions would be superimposed and hence could not be temporally ordered. It also

demonstrates conclusively that the nucleus of this galaxy can recover from and repeat an energy release of $\sim 10^{55}$ erg after a few million years.

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Absolute Frequency Measurement of the R(12) Transition of CO₂ at 9.3 μ m

THE frequency of a CO₂ laser stabilized to the R(12) transition of CO₂ has been measured with an accuracy better than one part in 10^9 . This is part of an experiment at the National Physical Laboratory to determine the speed of light to the full accuracy of the krypton-86 length standard¹.

Our result for the frequency of the CO₂ R(12) transition is

$$\nu = 32,176,079,482 \pm 28 \text{ kHz}$$

The provisional error comprises a random error of 4.2 kHz and possible systematic effects amounting to 27.5 kHz combined as the root sum of squares throughout. Further studies of these effects may reduce the error, which will be discussed in more detail elsewhere.

Comparison of the CO₂ laser frequency with the caesium standard at 9 GHz is achieved by harmonic generation and mixing of radiation from microwave, submillimetre wave and infrared sources, using point contact devices. The apparatus is an extension of that recently described for measurement of a stabilized H₂O laser frequency at 28 μ m (ref. 2). The CO₂ laser was stabilized to a saturated absorption dip observed using the 4.3 μ m fluorescence³ from an external CO₂ gas cell. The following three frequencies were measured concurrently. (i) The beat frequency between the CO₂ laser and the 3rd harmonic of a free-running 10.7 THz (28 μ m) H₂O laser; (ii) the beat frequency between the H₂O laser and the 12th harmonic of a free-running 891 GHz (337 μ m) HCN laser; and (iii) the HCN laser frequency via a klystron phase locked to the laser by fiftieth harmonic mixing in a Josephson junction.

A total of 480 readings in forty-eight sets of ten were obtained on five different days over a period of two months. Apart from the initial day (forty measurements) there were about 100 measurements per day with a standard deviation of a single reading near 60 kHz. Each set of ten was averaged and the standard deviation of the mean of these forty-eight averages was 4.2 kHz. The means of the four principal days were consistent to ± 4 kHz.

The chief causes of systematic error were: (a) possible asymmetry in the HCN laser spectrum causing a difference between time-averaged counting and the centre of the beat spectrum as observed and measured on a spectrum analyser; (b) uncertainties in the offsets produced by the servo-control system which locked the CO₂ laser to the dip in the saturated absorption signal from the CO₂ gas cell; (c) thermal drift of

the HCN laser frequency during the period of measurement (of the order of 1 s); (d) uncertainties in the relation of the local working frequency standard to the caesium standard.

After completion of our measurements and the foregoing analysis the result for the frequency of the CO₂ R(12) transition was communicated to the meeting of the Comité Consultatif pour la Définition du Mètre (June 14), and a comparison was made with the R(10) transition frequency measurement of K. M. Evenson *et al.*⁴ using a value for the R(12)–R(10) difference frequency recently determined at the National Bureau of Standards, Boulder. The agreement was within 3 parts in 10^{10} , and thus confirms one part of the frequency measurement by Evenson *et al.* in their determination of the speed of light⁵.

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Observation of Electron Swarms produced by Laser Light

OBSERVATION of the displacement current caused by the motion of charge carriers in a discharge gap can yield quantitative information on many basic processes¹, such as ionization, electron attachment and charge carrier mobilities. A relatively large number of charge carriers is, however, required to produce a signal which exceeds the high inherent noise level of any wideband detection system by a sufficient margin. Hitherto, it was necessary, except in one or two special cases, to rely on gas amplification to raise the electron current to an observable level; this is only possible, however, when ionization dominates attachment of electrons to neutral molecules. The number of initial electrons required is particularly high when measurements in electronegative gases (high voltage insulants such as SF₆ and air) are to be made over the technically important range of low ratios of field strength to pressure for which the electron loss by attachment is at least as probable as the production of additional electrons by ionization.

In order to apply relatively simple methods of electron current pulse shape evaluation, the primary electrons must be released from the cathode within a very short time; on the other hand, a high light intensity is required to produce a reasonable number of primary electrons. Attempts have been made to produce such a large number of primary electrons by ultraviolet light flashes (ref. 2 and references in ref. 1). With spark light sources, however, those two requirements contradict each other. Higher energy input tends to lead to a longer duration of the light emission; in particular, the light emission frequently shows a very long "luminosity tail" of lower intensity which can be troublesome in gas discharge studies. Attempts have been made

to eliminate the tail by means of an electro-optic shutter³, but the number of photoelectrons generated from normal cathodes by the shortened ultraviolet pulse (10^9) is far too small for many investigations. When the luminosity tail was not suppressed, primary electron numbers of about 10^6 within 20 ns were obtained from specially prepared cathodes in certain gases.

To overcome the drawbacks of spark light sources, we have used a Q-switched ruby laser with frequency doubling to generate an intense, short ultraviolet light pulse which has no tail. The fundamental and second harmonic frequency light beams are passed into a liquid filter to remove the red light which can cause thermionic emission. The ultraviolet beam is then expanded to illuminate a large central area of the cathode of a homogeneous field discharge gap. In this way, more than 10^8 photoelectrons can be generated within a well defined time interval less than 20 ns long. The displacement current set up by these electrons moving through the discharge gap is sufficiently high to permit direct recording with high time resolution even when the applied field is comparatively low. Thus the region of low field strength to pressure ratio, in which there is little or no ionization or even predominant attachment, becomes accessible for time-resolved current observation. In fact, measurements at ratios as low as 4 V m N^{-1} ($5 \text{ V torr}^{-1} \text{ cm}^{-1}$) have proved possible in CO_2 and permit determination of mean electron energies from the very pronounced influence of diffusion upon the pulse shape.

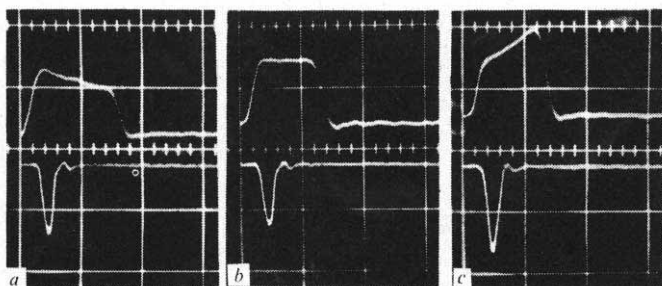


Fig. 1 Electron current pulses in carbon dioxide (pressure 12.8 kN m^{-2} , 96 torr) at different ratios of field strength to pressure: a, 10; b, 19; c, 21 V m N^{-1} ($14, 26, 28 \text{ V cm}^{-1} \text{ torr}^{-1}$). Top traces: current at $150 \mu\text{A}$ per principal division. Bottom traces: laser light intensity, time axis offset by 25 ns. Time scale in all cases 100 ns per principal division. For the conditions of a, attachment predominates ($\alpha - \eta = -31 \text{ m}^{-1}$); for b, attachment and ionization balance each other; for c, ionization predominates ($\alpha - \eta = +44 \text{ m}^{-1}$).

Typical current oscillograms for an electronegative gas are shown in Fig. 1. They allow the immediate determination of electron drift velocities and thus mobilities (from the pulse duration) and of the effective ionization coefficients $\alpha - \eta$, where α is the ionization coefficient and η the attachment coefficient. Trace (a) shows clearly the gradual reduction in the number of electrons due to attachment; the attachment coefficient η is here greater than the ionization coefficient α . The resulting negative ion current does not show in the oscillogram because of the much lower mobility of negative ions. A constant electron current which indicates equal values of ionization and attachment ($\alpha = \eta$) is shown as trace (b). Quite small changes in the field strength to pressure ratio ($< 2\%$) lead to a clearly discernible slope of the roof of the current pulse. Under the conditions of trace (c) the electron current is amplified by the predomination of ionization over attachment.

The observation of ion currents in all these conditions is well within the capabilities of the system and will yield all the information which could hitherto only be obtained in this way at the higher ratios of field strength to pressure. Such information and further details of parameters obtained from electron current pulse evaluation will be reported elsewhere.

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BIOLOGICAL SCIENCES

Genetic Transfer of the Stable L Form State to Intact Bacterial Cells

QUANTITATIVE mass conversion of bacteria to protoplasts and unstable L phase variants and the reverse process are probably not mutational events. The transition from unstable L phase variants to stable L phase variants, however, probably reflects a fundamental genetic change, although this is still in dispute¹. Increasing circumstantial biochemical data support this but genetic evidence is virtually non-existent. Several stable L phase variants, when compared with the protoplasts or bacteria from which they were derived by non-mutational induction procedures, are lacking in certain wall components^{2,3} and part of the DNA⁴, and possibly defective in stages of wall biosynthesis^{5,6}, and to possess altered membrane constituents^{7,8}, all of which may reflect an inability to carry out proper wall formation.

We used transformation to determine if the stable L state could be transferred to intact bacteria to result in the phenotypic expression of stable L forms. DNA from a stable L phase variant derived from *B. subtilis* 168 *trp* C2 (ref. 9) was isolated¹⁰ and used for transformation¹⁴. Saturating concentrations of DNA were used to transform competent cells of two recipients: M22 *pur* A16, *leu*-8, *met* B5, *ile*-1, and a streptomycin-resistant spontaneous mutant of 167 *trp* C2, *thy*, both of which were derived from *B. subtilis* 168 (ref. 11). Recombinants which were prototrophic for adenine and thymine were selected on DP agar plates (DPA)⁹, containing 0.5 M sodium succinate as an osmotic stabilizer and devoid of both horse serum and methicillin. A chemically defined medium SD (ref. 9), appropriately supplemented, was used to score the *pur*⁺ recombinants for retention of unselected amino acid markers. As L form colonies cannot be replica plated, individual L form colonies were excised from the isolation plates with a scalpel, mashed in sterile SD liquid medium, and aliquots of the suspension were spread on the appropriate plates to screen for unselected markers. Representative results are recorded in Table 1.

Transformation frequencies of 0.1–0.25% were routinely obtained for adenine recombinants. Three types of colonies were present on the initial selection plates: (1) *pur*⁺ bacterial colonies; (2) *pur*⁺ L forms (Fig. 1); and (3) a background growth of tiny colonies consisting of rods (Fig. 1a, b, arrows). The appearance of the latter colonies was probably the result of trace amounts of adenine contamination in the base medium. These tiny colonies presented difficulties in obtaining pure growth of many of the L forms on subculture, but it could be demonstrated that most of the L form transformants retained the auxotrophic markers of the recipient bacterium.

Transformation frequencies for thymine recombinants were 0.025%, 0.01% and 0.03%. Only two types of colonies were

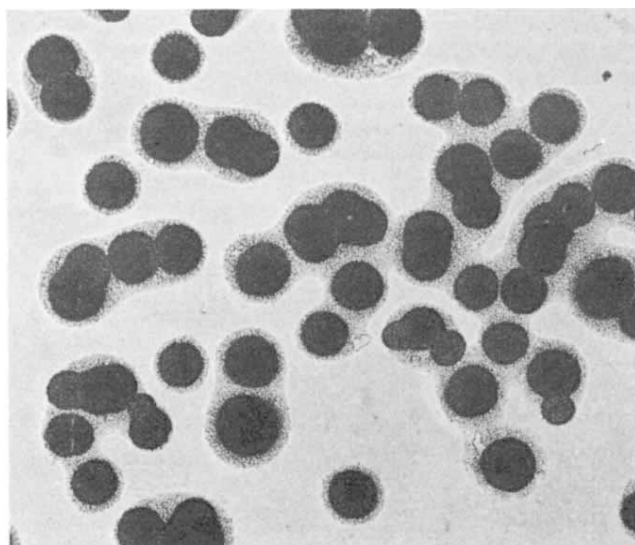
Table 1 Transformation of the Stable L Form State to Intact Bacterial Cells

Donor	Recipient	Selected marker	Transformant colonies ml ⁻¹	Co-transformation Marker	%
168 <i>trp</i> C2, S1f-1	M22 <i>pur</i> A16, <i>leu</i> -8, <i>met</i> B5, <i>ile</i> -1	<i>pur</i> ⁺	1.74 × 10 ⁶	<i>leu</i>	14
				S1f-1	9
168 <i>trp</i> C2, S1f-1	167 <i>trp</i> C2, <i>thy</i> <i>str</i>	<i>thy</i> ⁺	1.66 × 10 ⁶	<i>str</i>	8
				S1f-1	15

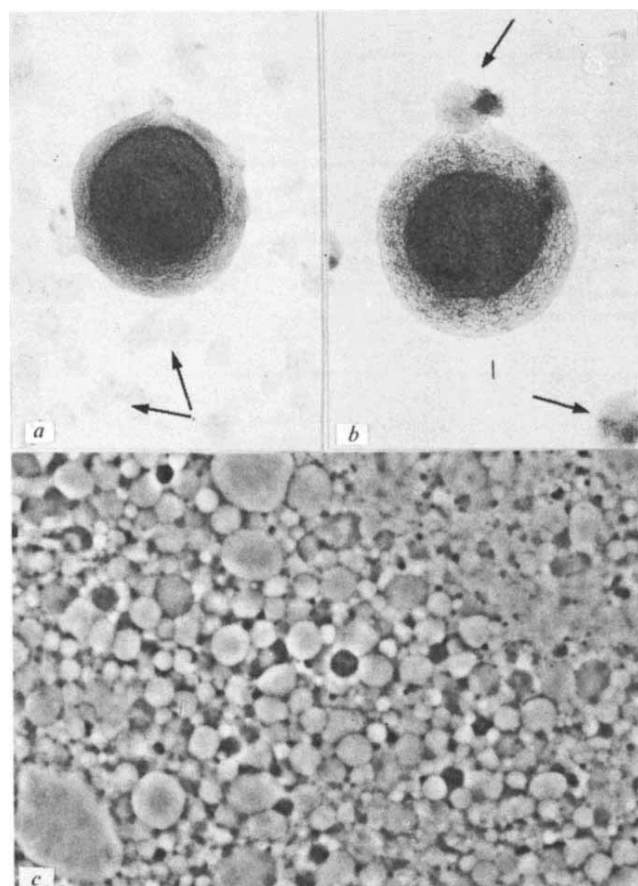
* S1f-1, phenotypic expression to denote stable L form, in accordance with the terminology recommended by Young and Wilson¹⁶ for morphological mutants.

present on the initial selection plates: (1) *thy*⁺ bacterial colonies, and (2) *thy*⁺ L forms. L forms obtained on subculture of an initial *thy*⁺ L form recombinant are represented in Fig. 2. Scoring of the L form recombinants for streptomycin resistance was performed on DPA containing 1,000 µg ml⁻¹ streptomycin. These L forms were also tested for their stability by their ability to grow as L forms on DP medium containing 2.5% agar and DP medium supplemented with 25% gelatin. The results are recorded in Table 2.

In all the transformation experiments performed the number of L forms obtained represented approximately 10% of the total number of transformants. Inoculation of the recipient bacterial cells alone on DPA never resulted in the appearance of

**Fig. 2** L forms obtained on subculture of an initial *thy*⁺ L form recombinant.

L forms. Further proof that the L forms were derived from the recipient cells was demonstrated by the retention of recipient markers. It may be concluded therefore that the L form colonies arose as a direct result of genetic transformation. The stability of the L form transformants was demonstrated by their inability to revert to the classical bacterial phase on hard agar or medium supplemented with 25% gelatin^{12,13,15}. Our study clearly demonstrates that this stable *B. subtilis* L phase variant, eventually obtained from initial treatment of the parent

**Fig. 1** Individual *pur*⁺ recombinant L form colonies on initial selection plates. *a* and *b*, Low power photomicrographs reveal L form colony morphology: a dense centre surrounded by a vesicular periphery; magnification × 63. The arrows point to background growth of small colonies, consisting of rod cells, which arose probably as a result of trace amounts of adenine in the base medium. *c*, High power photomicrograph of L phase variant cells in an L form colony; magnification × 1,000.**Table 2** Scoring of L Form *thy*⁺ Recombinants for Streptomycin Resistance and Stability

L Form <i>thy</i> ⁺ recombinants	Streptomycin resistance	Reversion to bacterial phase	
		2.5% agar	25% gelatin
AA1	+	0	0
AB1	+	0	0
AC2	+	0	0
AC3	+	nd	0
CA5	+	0	0
CB2	+	nd	nd
CC1	—	nd	0
CC3	+	0	0
CC4	—	0	nd
C41	+	0	0
Control L phase variant	—	0	0

—, No growth; 0, no reversion, growth as L forms; +, growth; nd, not done.

bacterial cell population with lysozyme, is a mutant and that the characteristic responsible for the stable L state can be transferred to an intact bacterial cell with the resultant recovery of a stable L form.

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Cascade Activation of Genome Transcription in Wheat

TRANSCRIPTIONAL events are arrested in developing plant seeds when maturation is completed. The RNA synthesis may be resumed when suitable changes in the environment make it possible for the seed to germinate. It is not known, however, how early and in what order the synthesis of cellular RNA species is activated in response to the stimulus to germinate. Our previous observations^{1,2} indicate that RNA synthesis is triggered almost immediately before the activation of protein synthesis *in vivo* but other reports³⁻⁵ suggest that RNA synthesis remains repressed for many hours after germination starts. Further attempts to establish the time course of RNA synthesis in germinating wheat embryos were therefore undertaken.

The seeds of wheat, *Triticum aestivum*, were labelled with ¹⁴C-uridine and germinated as described (Fig. 1). The precursor was incorporated into the embryo RNA from the onset of germination, but the rate of incorporation was not constant throughout the investigated period (Fig. 1). There was a rapid phase of RNA synthesis (0 to 3 h), followed by a levelling (3 to 12 h) after which the synthesis resumed linearly. The levelling could not result from a dilution of the precursor by the endogenous uridine. The considerable drop in specific radioactivity of uridine was found to occur in the embryo only 12 h after germination started.

The biphasic time course of uridine incorporation (Fig. 1) seems to indicate that RNA synthesis is activated in the germinating wheat embryos in a stepwise manner. The first activation step results, probably, in only limited RNA synthesis. This initial activation begins immediately after ger-

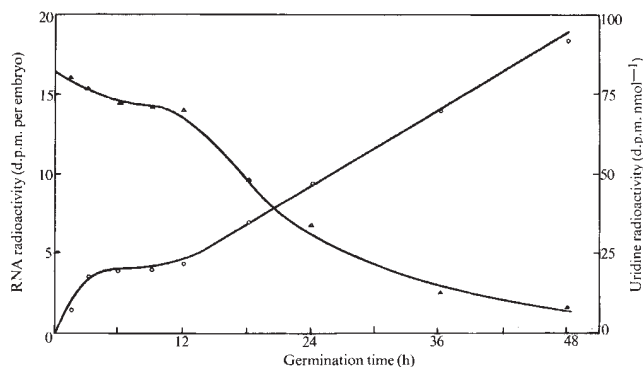


Fig. 1 Time course of ¹⁴C-uridine incorporation into wheat embryo total RNA during germination. A sample of 250 wheat grains was surface sterilized with 2% NaClO, immersed in 10 ml of ¹⁴C-uridine solution (0.03 μ Ci ml⁻¹, 0.6 μ Ci μ mol⁻¹) at 2° C for 8 h and then allowed to germinate at 22° C. After the requisite germination period, embryos were separated manually from the remaining parts of the grains and used for the isolation of total RNA and uridine. Total radioactivity of the isolated RNA (○) and specific radioactivity of the isolated uridine (△) were then determined¹.

mination starts, and is apparently completed within the first 3 h. Further activation does not begin until 12 h after the start of germination. The second activation step probably leads to the full activation of cellular RNA synthesis.

It seemed desirable to compare RNA species synthesized in conditions of limited activation with those appearing after the activation is fully completed. Distribution of the newly synthesized (labelled) polynucleotides among mRNA, rRNA and tRNA fractions was therefore studied as a function of the germination time. The α variant mRNA fraction was isolated according to the method of Weeks and Marcus⁶. After preliminary screening experiments, the methods of Caldwell and Henderson⁷ and Delihis and Staehelin⁸ were chosen for the isolation of rRNA and tRNA fractions, respectively. The recoveries of the added labelled rRNA and tRNA were checked and found to be satisfactory (75 to 85%). It was shown that the initial activation of RNA synthesis results in the labelling of mRNA fraction only (Table 1). The second activation step probably corresponds to the initiation of rRNA synthesis. Significant radioactivity appeared in this fraction after 12 h germination and increased considerably thereafter. Soon after the rRNA synthesis began, the third activation step, manifested by the labelling of the tRNA fraction, occurred. The tRNA fraction contributes little to the total RNA radioactivity (15% after 24 h germination) and, for this reason, the last activation step cannot be distinguished from the incorporation curve (Fig. 1).

The sequential labelling of mRNA, rRNA and tRNA fractions may suggest an ordered derepression of the genome, provided that the mRNA fraction does not contain rRNA precursor (or tRNA precursor) molecules. To distinguish between mRNA and rRNA precursor molecules, the nucleotide composition of the newly synthesized RNA was determined with the use of ³²P_i as the precursor. It was found that the early RNA is rich in U+G and is unlike the total RNA of the dry or germinated embryos. The low CMP content (14.8 mol%) does not indicate an early rRNA synthesis and does not confirm the recent finding of Chen *et al.*⁹ although the base composition found here for the early synthesized RNA is similar to that of RNA present in the messenger fraction of the wheat embryo². The early RNA differs from most mRNAs in its low AMP content. Histone mRNAs, however, do not contain poly (A) sequences^{10,11}. A need for histone mRNA synthesis in the embryos may be expected, as a burst of histone synthesis has been observed in a similar system¹².

The mRNA fraction, isolated from wheat embryos according to the method of Weeks and Marcus⁶, is obtained as a

Table 1 Incorporation of ^{14}C -Uridine into mRNA, rRNA and tRNA and Fractions of Germinating Wheat Embryos

Germination time (h)	Messenger fraction		RNA (amount and radioactivity)		Transfer fraction	
	(mg per 100 embryos)	(d.p.m. mg^{-1})	Ribosomal fraction (mg per 100 embryos)	(d.p.m. mg^{-1})	(mg per 100 embryos)	(d.p.m. mg^{-1})
0	0.05	< 50	1.30	< 10	0.60	< 10
0.75	0.04	1,050	1.35	< 10	0.62	< 10
1.5	0.04	3,800	1.30	< 10	0.62	< 10
3	0.05	7,350	1.23	< 10	0.60	< 10
6	0.06	6,100	1.26	< 10	0.51	< 10
12	0.06	4,250	1.32	190	0.40	< 10
24	0.08	1,400	1.58	430	0.45	360
48	0.08	850	1.77	710	0.73	740

Wheat grains were labelled and germinated as described in the legend to Fig. 1. The RNA fractions were isolated from the embryo moiety of the grain according to methods quoted in the text.

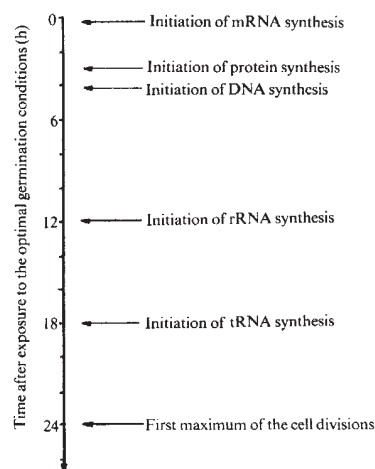
nuclear ribonucleoprotein complex, sedimenting at 39,000g. When the pellet was resuspended in the extraction buffer⁶, layered on a 10 to 30% sucrose gradient and centrifuged at 85,000g for 2 h, the material absorbing at 260 nm sedimented heterogeneously between 40S and 200S. The isolated material was rapidly degraded to 40S particles after 6 h storage at 0° C. The 40S particles were composed of protein and RNA in a mass ratio of 4:1. Only the RNA component was radioactive in the 40S RNP particles isolated from embryos labelled with both ^{14}C -uridine and ^{14}C -leucine and germinated for 3 h. This indicates that the newly synthesized RNA combines, within the cell nucleus, with a pre-existing protein component. The resulting RNP particles may be compared with informosomes known from other studies¹³. Although the ultimate characterization of the mRNA fraction must await the identification of the proteins that it codes for, all the data so far available are consistent with the assumption that this fraction is similar to nascent mRNA-protein complexes known to occur commonly in other eukaryotic cell nuclei.

Table 2 Nucleotide Composition of Total and Newly Synthesized RNA of Germinating Wheat Embryos

Germination time (h)	Nucleotide proportions (mol %)							
	AMP	Total RNA GMP	CMP	UMP	AMP	Newly synthesized RNA GMP	CMP	UMP
0	23.5	31.1	24.8	20.6	—	—	—	—
3	21.2	32.0	24.3	22.5	11.4	36.5	14.8	37.3
48	22.7	30.9	24.8	21.6	22.8	29.3	25.8	22.1

Wheat grains were labelled and germinated as described in the legend to Fig. 1, except that ^{32}P -orthophosphate (1 mCi) was used as the radioactive RNA precursor. Mononucleotides resulted from alkaline hydrolysis of the wheat embryo RNA were separated by column and paper chromatography². Base composition of the newly synthesized RNA was calculated from ^{32}P distribution among the isolated nucleotides.

We conclude that the transcriptional events are activated in a cascade manner after the wheat embryo is exposed to optimal germination conditions. Cascade activation requires RNA synthesis to reach some initial level soon after the start of germination and to cease to rise further until the next activation step, after which the synthesis proceeds with greater intensity. Three successive activation steps were recognized and shown to be concerned with the initiation of mRNA, rRNA and tRNA synthesis, in that order. These, and previously reported observations^{1,2} on DNA, RNA and protein synthesis in germinating wheat embryos, as well as mitotic index data obtained for the same material (J. Eberhardt, personal communication), are included in a scheme illustrating the sequence of major biosynthetic events trig-

**Fig. 2** The sequence of major biosynthetic events triggered in the wheat embryo during early germination.

gered at germination (Fig. 2). This sequence is similar to that induced in animal cells in response to the stimulus to proliferate¹⁴⁻¹⁶.

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Involvement of a Carbohydrate Group in the Active Site for Surface Guided Reassociation of Animal Cells

THE coordinated cell interactions which occur during development are thought to be due to molecular gradients throughout critical tissue zones¹ or to specific cellular adhesions^{2,3}. A model system of the latter was described in 1907 by H. V. Wilson^{4,5} who dissociated a yellow and a red species of marine sponge, mixed the cell suspensions and found that the cells sorted into species specific aggregates of the two separate colours. Such sorting out occurs also in embryonic vertebrate cells⁶ and was found to be organ specific³. Specific reaggregation and sorting out are assumed to be guided by specific macromolecular components of the cell surface. Surface components have been obtained from chick neural retina⁶ and mouse cerebrum⁷ which preferentially enhance the aggregation of cells from the homologous tissue.

The species specific reaggregation of sponge cells observed by Wilson is mediated by a similar factor (aggregation factor, AF) released from the sponge cell surface⁸⁻¹⁰. Studies of AF indicate that it is a high molecular weight glycoprotein which requires Ca^{2+} for biological activity^{11,12}. Preliminary evidence from this laboratory suggested that specific carbohydrates are directly involved as determinants of the specificity of AF from at least one species of sponge¹³. We report here further studies into the involvement of carbohydrates in the aggregation-enhancing activity of *Microciona prolifera* AF.

The high proportion of carbohydrate present in AF, as well as its sensitivity to periodate (5 mM at 4° C for 12–15 h), suggest that carbohydrates may be involved in AF activity. Therefore we tested the ability of the carbohydrates commonly found in glycoproteins to inhibit AF activity (Table 1). Only glucuronic acid was an effective inhibitor and the

inhibition was only observed when chemically dissociated cells were pre-incubated with glucuronic acid and then AF was added. When the order of addition was reversed inhibition was rarely observed. This suggests that glucuronic acid residues present in AF are important for *M. prolifera* AF activity. The involvement of glucuronic acid in AF action is not a general property of sponge AF, as glucuronic acid had no effect on the aggregation of a second species (*Cliona celata*) by its AF.

Uronic acids are known to bind Ca^{2+} and AF requires Ca^{2+} for activity⁸. Therefore we tested the possibility that glucuronic acid inhibition of AF is due only to its ability to bind Ca^{2+} . We attempted to overcome glucuronic acid inhibition of aggregation by the addition of Ca^{2+} to chemically dissociated cells before the addition of AF. Glucuronic acid inhibited aggregation even when a three-fold molar excess of Ca^{2+} was added, while galacturonic acid and glucose had no effect on aggregation even when the latter sugars were present at twice the molar concentration of Ca^{2+} . Furthermore, titration experiments (Radiometer, Copenhagen) which easily demonstrated Ca^{2+} binding by EDTA did not indicate Ca^{2+} binding by glucuronic acid at a Ca^{2+} to glucuronic acid ratio of 6:1 and 3:1.

Table 2 Effects of Glycosidase Digestion on AF Activity

Enzyme digestion of AF	Degree of aggregation
Control without glycosidase	4+
Glycosidase added	0
Glycosidase + 0.1 M glucuronic acid	4+
Glycosidase + 0.1 M glucose galacturonic, sialic acid or N-acetylglucosamine	0

Crude *Helix pomatia* enzyme (Endo Labs, Long Island) was diluted to a final concentration of 240 U ml⁻¹ with 0.1 M Tris buffer (pH 7.7) containing 10 mM CaCl_2 . The enzyme preparation was incubated for 2 h at room temperature with AF diluted to a final protein concentration of 80 µg ml⁻¹. Carbohydrates were added to the glycosidase preparation before the addition of AF. The digests were chilled in ice, dialysed overnight in 100 volumes of ice-cold seawater and tested for AF activity. The aggregation assay was conducted for 20 min at room temperature in 3 ml total volume of seawater containing approximately 10⁷ cells and 2.5 ml of the digest. Control experiments indicated that the glycosidase present in the aggregation assay did not cause the aggregation of CMF cells in the absence of AF.

Digestion of AF by a non-specific glycosidase preparation from *Helix pomatia* also inhibited AF activity (Table 2). End-product inhibition of a similar non-specific preparation has been used to define the carbohydrate involved in lympho-

Table 1 Inhibition of *M. prolifera* AF Activity by Carbohydrates

Carbohydrate	Concentration (mM)	Degree of aggregation	Carbohydrate	Concentration (mM)	Degree of aggregation
None	—	4+	Glucose	50	4+
Cells only, no AF	—	0+	Galactose	50	4+
Glucuronic acid	5	4+	N-Acetylglucosamine	50	4+
Glucuronic acid	25	2+	N-Acetylgalactosamine	50	4+
Glucuronic acid	100	1+	α-Methyl-glucose	50	4+
Cellobiuronic acid	5	2+	α-Methyl-mannose	50	4+
Cellobiose	50	4+	Mannose	50	4+
Galacturonic acid	50	4+	Fucose	50	4+

Chemically dissociated cells and AF were prepared by the methods developed by Humphreys⁸. All AF preparations were 105,000g pellets resuspended in complete artificial seawater¹⁷. Chemical analyses indicated hexose to protein ratios of 51:49, in good agreement with earlier reports of sugar to protein ratios for *Microciona* AF of 1:1 (ref. 12). In addition, we found that 15% of the hexose consisted of uronic acids. The carbohydrates indicated were preincubated for 5 min at room temperature in a 25 ml Erlenmeyer flask containing 2–5 × 10⁷ cells in 2 ml of seawater. 1 ml of seawater containing AF preparation (30 µg ml⁻¹ protein) was then added and the degree of aggregation scored after 20 min of rotation at room temperature (36 r.p.m., 4 cm diameter circle). Aggregation was determined according to the following scale: 4+ = one to five clumps; 3+ = five to 100 clumps; 2+ = 100–5,000 clumps; 1+ = fine granulation and distinguishable from 0; 0 = no visible granulation.

Concentrations of carbohydrates given are the final concentrations during incubations. Uronic acids and derivatives were buffered to pH 7.0 with NaOH.

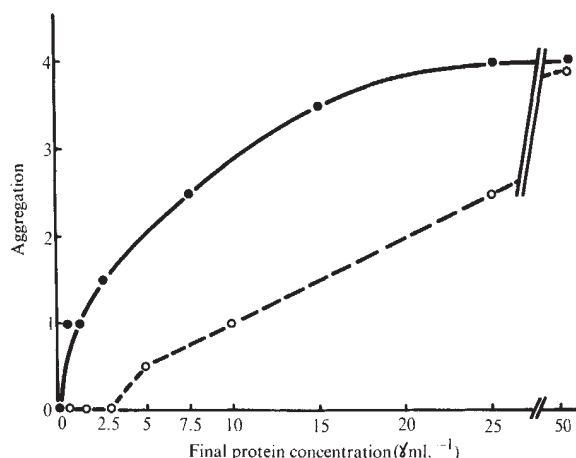


Fig. 1 Aggregation of *M. prolifera* cells by *M. prolifera* AF (●) and by *Haliclona occulata* AF (○). The original protein concentration of the *Microciconia* factor preparation was 750 μg ml⁻¹ and the *Haliclona* factor preparation contained 150 μg ml⁻¹ of protein, which means that adding 0.10 ml of each factor brings the final protein concentration to 5 μg ml⁻¹ in the case of *Haliclona* factor and 25 μg ml⁻¹ in the case of *Microciconia* factor. The degree of aggregation indicated was attained in 20 min at 22° C, aggregation did not occur in the absence of factor, and there was no significant increase in aggregation during the subsequent 60 min. The greater efficiency of *Microciconia* factor relative to that of *Haliclona* factor for *Microciconia* aggregation was observed when readings were taken before 20 min. Instead of the two-fold higher specific activity (based on protein concentration of the factor preparations) a 3–5-fold better efficiency was observed for the homotypic (*Microciconia* factor and *Microciconia* cells) against the heterotypic (*Haliclona* factor and *Microciconia* cells) combination of factor and cells.

cyte homing¹⁴. End-product inhibition of the *Helix* enzyme by glucuronic acid, but not glucose or galacturonic acid, during treatment of AF with the non-specific enzyme protected AF from digestion by the glycosidase preparation. The effect of *Helix pomatia* glycosidases on AF activity is thus probably due to the removal of glucuronic acid from AF. These experiments lead us to conclude that *Microciconia* AF contains glucuronic acid residues which are directly involved in mediating the reaggregation of *Microciconia* cells.

Direct proof of this conclusion demands isolation and complete chemical analysis of AF fragments which inhibit AF activity. We have begun such experiments and preliminary studies lead to some specific low molecular fragments isolated on a 'Sephadex' column from a pronase digest which were strong inhibitors and have a very high carbohydrate to protein ratio.

The reaggregation of *Microciconia* cells has been reported to occur in a species specific fashion⁸. As a preliminary experiment to investigations on the specificity of *Microciconia* AF, we tested the ability of *Microciconia* AF and *Haliclona occulata* AF to aggregate *Microciconia* cells. We observed (Fig. 1) that both AF preparations were able to mediate aggregation, although the *Haliclona* AF was only 10% as effective as *Microciconia* AF on a volume basis and less than 50% as efficient when the comparison is based on protein content. This preliminary observation suggests that species specific reaggregation is based on quantitative, as well as qualitative, differences between the surface properties of these two species of sponge. The apparent contradiction in reports (for example ref. 16) that mechanically dissociated cells show species specific reaggregation, but that AF preparations from the same species are not specific, may, in some cases, be resolved by experiments (such as described in Fig. 1) which investigate the qualitative and quantitative aspects of the interaction of chemically dissociated cells with AF from both the homologous and heterologous species.

Previous studies on sponge cell aggregation have indicated

that aggregation factor is inactivated by periodate oxidation¹¹ as well as by protease treatment¹¹. We have here proved that carbohydrates can provide specificity to the action of AF. Although inactivation by proteolytic enzymes seems to argue against carbohydrates as the source of specificity, the model in ref. 15 explains such observations as it suggests that the protein is the structural carrier of the carbohydrate groups involved in specificity (Fig. 1, ref. 16). This working model is being used as a guide for our future research and will be revised as more evidence is obtained concerning the mechanism of aggregation factor mediated sponge cell reaggregation.

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Two Component System for Surface Guided Reassociation of Animal Cells

SPONGE cells dissociated by means of seawater containing no calcium or magnesium release a large molecular factor (AF) which is required for specific reaggregation at 4° C into multicellular agglomerations the size of small sponges¹. The function of the aggregation factor (AF) in *Microciconia prolifera* is dependent on a specific carbohydrate². Here we describe the isolation of a second macromolecular component, other than AF, which is necessary for reaggregation, and which seems to remain on the surface of the cell after removal of the aggregation factor, and to interact with intercellular AF. Until its function is clearly understood, we shall describe it as a baseplate.

Earlier we found that hypotonic treatment of cells can release components from the surface of tumour cells³. Chemically dissociated (2×10^6) *M. proliferans* cells treated with 0.09–0.07 M NaCl at 37° C for 30 min completely lost the ability to aggregate in the presence of AF (Table 1, experiments 7 and 4). The medium from the hypotonic shock treatment contained a heat labile, pronase sensitive, non-dialysable component that could not be pelleted at 105,000g or extracted as a lipid⁴ and which was capable of inducing aggregation in shocked cells if added simultaneously with AF and calcium (Table 1, experiments 6–9). Hypertonic shock (3 M NaCl) did not lead to the removal of such a component. If this component has acceptor function for the AF, that is if it acts as a baseplate, it should bind to cells which lack it and only then should such cells be responsive to AF. Addition of the baseplate fraction to hypotonically treated cells, even in the absence of calcium or AF, and subsequent removal of the incubation medium and addition of AF led to aggregation. Reversing the order of incubation with AF and baseplate did not result in aggregation. Simultaneous addition of preincubated AF and baseplate fractions also restored aggregation (Table 1, experiment 9).

Table 1 Whole Cell Aggregation Studies using *M. proliferans*

Experiment No.	Cell type used	AF added	Baseplate added	Glu-COOH added	Degree of aggregation
1	Mech	—	—	—	4+
2	Mech	+	—	—	4+
3	CMF	—	—	—	—
4	CMF	+	—	—	4+
5	CMF	—	+	—	—
6	CMF+Hy	—	—	—	—
7	CMF+Hy	+	—	—	—
8	CMF+Hy	—	+	—	—
9	CMF+Hy	Preincubated	—	—	3+
10	CMF+Hy	Second	First *	—	3+
11	CMF+Hy	First *	Second	—	—
12	CMF	Preincubated	—	—	—
13	CMF	Second	First †	—	—
14	CMF	First †	Second	—	4+
15	Mech	—	+	—	2+
16	CMF+Hy	Second	Preincubated	—	—
17	CMF	Second	Preincubated	—	4+
18	CMF	Second	—	First †	—
19	CMF	+	—	+	4+
20	Mech	—	—	+	—

The incubation mixture included: 0.05 ml AF², 0.3 ml baseplate (about 700 µg protein ml⁻¹), 5×10^{-2} M glucuronic acid (Glu-COOH) final concentration, and seawater to bring the volume to 2.0 ml. The reaction was started by addition of 1.0 ml of sponge cell suspension (5×10^7 cells ml⁻¹). CMF, chemically dissociated²; Mech, mechanically dissociated; CMF+Hy, chemically dissociated, then hypotonically shocked cells. Readings were taken at 15 min after initiation of shaking at room temperature. Scorings were as in the previous report².

* Added to cells either in calcium-magnesium free seawater or in calcium-magnesium free seawater to which 2×10^{-3} M Ca²⁺ was added. Cells were then spun for 90 s at 1,000 r.p.m., re-suspended in calcium-magnesium free seawater and the second reagent added.

† First reagent was in contact with cells for 5 min; only then was the reaction started with second reagent.

Further evidence for a direct interaction between AF and baseplate activity came from the following experiment. The baseplate preparation was capable of inactivating AF, presumably by binding to it, if the two were preincubated and then added to unshocked, chemically dissociated cells which still carried their baseplate (Table 1, experiment 12). The order of addition, however, was again important (Table 1, experiments 13 and 14).

Further support for the concept that baseplate material binds to AF comes from another inhibition experiment. Mechanically disrupted cells still carry enough AF on their surface to aggregate in seawater containing calcium. Baseplate material should bind to the AF on such cells and

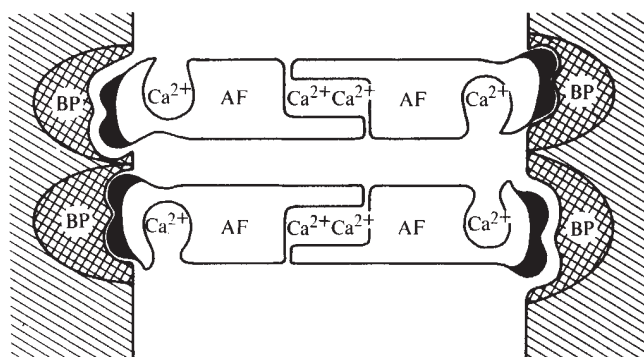


Fig. 1 Tentative model for specific cell-cell interactions in tissue construction. Two macromolecular AFs are illustrated each consisting of at least two subunits. The black termini at each pole carry the carbohydrates, which are recognized by the baseplate (BP) anchored in adjoining cell surfaces.

inhibit aggregation as can indeed be seen in experiment 15 of Table 1, if compared with experiment 1.

The apparent role of glucuronic acid is as a recognition site on AF, necessary for AF baseline binding, as described in the previous paper². This suggestion is strengthened by the fact that the baseplate fraction is rendered non-functional if preincubated with glucuronic acid, both for direct activity measurements with cells lacking both AF and baseplate (Table 1, experiments 16 and 10) as well as for inhibitory experiments with cells lacking only AF (Table 1, experiments 17 and 13). Further support comes from experiments 18 and 19 in which glucuronic acid inhibited aggregation of cells in the absence of AF but still containing baseplate, if it was preincubated with, and capable of binding to, the baseplate before AF was added and not if added together with AF.

In an effort to obtain a cell-free test system either AF or an AF free baseplate fraction was covalently attached to 'Sephacrose' beads⁵. When AF coated beads were added to a suspension of chemically dissociated cells, the cells bound to the beads. If AF beads were added to hypotonically shocked, chemically dissociated cells, the cells had no affinity for the beads. Similarly, baseplate beads bound only shocked cells but not chemically dissociated cells. Such results suggest that the beads might be used as an acellular aggregation system.

The results of aggregation experiments with coated beads are shown in Table 2. It is clear that AF beads act similarly to mechanically dissociated cells (Table 2, experiments A–C; and Table 1, experiments 1, 2, 15 and 20), with the exception that glucuronic acid inhibits aggregation of mechanically dissociated cells but does not affect AF beads. This is to be expected because AF beads bind only by factor:factor interaction, while the mechanically disrupted cells (where some of the disruptions have occurred between AF and baseplate) interact primarily by factor:baseplate binding (see model below). It also seems that beads coated with baseplate act similarly to chemically dissociated cells (Table 2, experiments D–I; and Table 1, experiments 3–5, 12, 18, 19).

In an effort to use AF beads to purify baseplate activity by affinity chromatography we found in preliminary experiments that all baseplate-like activity was bound to an AF bead column and none to an unsubstituted column of activated beads. Figure 1 summarizes our observations from this and the previous paper in a tentative model. The salient points are the following. (1) Aggregation requires two different components, an intercellular aggregation factor (AF) and a baseplate (BP) anchored within the cell surface. (2) The AF is a multicomponent and multivalent macromolecular complex of carbohydrates and protein. One unit contains among other components at least two, probably several, identical subunits involved in the recognition process. (3) In the

sponge cell interaction examined, carbohydrate on the AF seems to be recognized as an antigen by a surface protein serving as an antibody-like baseplate for the AF. In calcium-magnesium free seawater removal of small amounts of calcium will loosen up peripheral attachment points of the AF and lead to its release. Prolonged incubation in calcium-magnesium free seawater or incubation in EDTA will eventually remove tightly bound calcium and inactivate AF. Mechanical dissociation of cells randomly disrupts AF-baseplate interactions on two adjoining cell surfaces. Among many possibilities this might be due to a certain asymmetry in anchorage of the AF as illustrated symbolically by different gap widths between the carbohydrate end of AF and the baseplate.

Table 2 Bead Aggregation Studies using 'Sephacrose' 4B Beads to which *M. prolifera* AF or Baseplate (BP) has been Covalently Linked⁶

Experiment No.	Beads added containing	AF added	Baseplate added	Glu-COOH added	Degree of aggregation
A	AF	—	—	—	3+
B	AF	—	+	—	—
C	AF	—	—	+	3+
D	BP	—	—	—	—
E	BP	+	—	—	4+
F	BP	—	+	—	—
G	BP	Preincubated	—	—	—
H	BP	Second	—	First*	—
I	BP	First*	—	Second	4+
J	AF+BP	—	—	—	4+

The reaction mixture is the same as in Table 1 except 0.05 ml bead suspension in calcium-magnesium free seawater replaces 1.0 ml of sponge cell suspension. Aggregation of the beads was almost immediate after addition of calcium-containing seawater (10 s to 2 min). The extent of aggregation was scored on the following scale: 4+ showed 90% of the beads in a single clump; 3+ 90% of the beads as two to ten clumps; 2+ showed 90% of the beads as eleven to 200 clumps; 1+ showed 90% of the beads as microscopic clumps each of more than five beads.

* First reagent was in contact with beads for 2 min. Only then was the second added and the degree of aggregation measured 2 min after the second addition.

We should like to advocate the use of beads covered with cell specific surface components as model systems for the study of some embryological cell-cell interactions. Whether such studies will be applicable to organogenesis in general and to other specific morphogenetic interactions in mammalian cells during differentiation is not yet clear. Our semi-quantitative studies will now have to be put on solid quantitative and biochemical grounds and the species specificity of both AF and baseplate activity will have to be investigated.

A preliminary note of part of this work was published previously⁶. Since then Dr T. Humphreys has informed us that he has isolated a component similar to the baseplate material by another technique.

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Recognition of Protein Structure in Leukocyte Chemotaxis

RECOGNITION of antigen in the specific immune response is well understood. Recognition of foreign or altered self material by the cells which mediate non-specific immunity has received little attention. In tissue injury or bacterial infections, many proteins may become enzymatically degraded or conformationally altered. Here I report a study of the chemotactic migration of neutrophil leukocytes towards the model proteins, haemoglobin and myoglobin, in their native and haem-free conformationally altered forms, and show that conformational changes in these proteins are recognized by leukocytes and evoke a chemotactic response, although the native proteins are inactive. A model for the molecular basis of this recognition is proposed.

Haemoglobin was prepared from normal adult human red cells by the method of Rossi-Fanelli *et al.*¹ and myoglobin (horse heart) and haemin were purchased from B.D.H. Ltd, Poole, Dorset. Neutrophil leukocytes were obtained from the leukocyte-rich plasma after dextran sedimentation of heparinized normal human blood. Monocytes were separated from these on 'Ficoll-trisil'. The chemotactic technique used was as previously described². Migration was quantified by measuring the distance migrated through a micropore filter in a fixed time by the leading front of cells³. Globin (apohaemoglobin or apomyoglobin) was prepared from haemoglobin and from myoglobin by the cold acid-acetone method of Rossi-Fanelli *et al.*⁴. Haemoglobin or myoglobin was reconstituted from apohaemoglobin or apomyoglobin by addition of haemin as described previously⁵. The formation of globin and the reformation of haemoglobin or myoglobin were measured by changes in the absorption intensity of the spectrophotometric peak in the Soret region (406 nm for haemoglobin: 409 nm for myoglobin).

Table 1 Chemotactic Migration of Human Neutrophils towards Various Preparations of Human Haemoglobin and Horse Myoglobin

Sample at 1 mg per ml and pH 7.2	Neutrophil migration (μm) in 75 min in 3 μm pore size filters
Oxyhaemoglobin	31
CO haemoglobin	38
Reduced haemoglobin (Na ₂ S ₂ O ₄)	28
Ferrihaemoglobin	37
Apohaemoglobin	93
Myoglobin (Fe ^{III})	30
Apomyoglobin	76
Gey's solution (suspending medium for all tests, negative control)	22
Casein 5 mg ml ⁻¹ (positive control)	105

Table 1 shows that the conformational changes in haemoglobin associated with binding of ligands, such as O₂ or CO or with the change from the ferrous to the ferric state, did not make the protein significantly chemotactic, but when haem was removed from haemoglobin or myoglobin, the resulting globin solutions were chemotactic for human blood neutrophils and monocytes (data not shown). A

drop in helical content of from 65% to 52% α helix for haemoglobin⁵, and a similar drop for myoglobin^{6,7} took place on removal of haem. As it was possible that the acquisition of chemotactic activity on the formation of globin was due to recognition by leukocytes of this loss of folded structure in the protein, and as the unfolding which accompanies the formation of globin can be completely reversed by readdition of haemin to globin to form a haem protein structurally identical to the original native form⁵⁻⁷, experiments were performed to see whether this refolding was accompanied by loss of chemotactic activity. This proved to be so. Figure 1 shows that the chemotactic activity of apohaemoglobin is progressively reduced as increasing amounts of haemin are added to the protein. At a ratio of one mol of bound haemin per mol of globin dimer, a ratio at which the native form is fully recovered⁵, the chemotactic activity is essentially that of the original haemoglobin. Similar results were obtained on addition of haemin to apomyoglobin. The reversible chemotactic activity of haem proteins is, therefore, probably due to recognition of leukocytes of reversible conformational changes in the protein molecule.

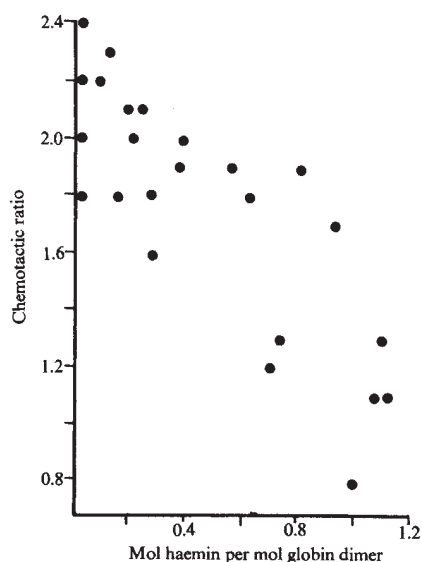


Fig. 1 The chemotactic activity for human neutrophils of apohaemoglobin combined with haemin at varying molar ratios. The chemotactic ratio was taken as the migration (μ m per 75 min) towards test sample against the migration towards native ferrihaemoglobin. Note that as the molar ratio of bound haemin is increased, the chemotactic activity of the protein decreases.

In previously reported experiments², it was shown that when a protein such as human serum albumin (HSA) was conjugated to various synthetic side groups, non-polar groups, such as tosyl, propionyl or butyryl groups, made the protein more chemotactic for neutrophils than did polar side groups. It was suggested that the chemotactic activity of those conjugated proteins was due to recognition by the leukocyte of externally positioned non-polar groups on a protein molecule. Those experiments also showed that this recognition was unlikely to result from the presence on the leukocyte of a stereospecific receptor for chemotactic factors, as migration of leukocytes towards a protein conjugated to a given side group was not inhibited by the presence of the conjugated substance in excess in free solution. It is likely that the same recognition mechanism may serve for chemotaxis towards denatured proteins as, in native haemoglobin and myoglobin, the non-polar residues are packed into the interior of the molecule but are

forced to the exterior when haem is removed. Experiments with HSA⁸ have indicated that polymerization of denatured proteins is not necessary for chemotactic recognition but that leukocytes migrate towards denatured proteins in their monomeric form. Therefore, these cells detect conformational changes in proteins without a requirement for stereospecific binding by a receptor. The presence of external non-polar groups on proteins in the environment of the leukocyte might provide a suitable marker leading to a cellular response which results in removal of the damaged protein.

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Tetraploid Mouse Embryos produced by Cytochalasin B during Cleavage

It has been reported that cytochalasin B can prevent cytokinesis without influencing nuclear division¹. Cells undergoing mitosis in the presence of cytochalasin B become binucleate and occasionally, with prolonged incubation, multinucleate¹⁻³. Treated cells generally resume cleavage upon removal from cytochalasin and reculturing. It has been shown that many of the binucleate cells produced in a BHK21 cell line will develop as tetraploids upon reculturing in fresh medium^{4,5}. Here I report the treatment of cleaving mouse eggs with cytochalasin and the establishment of tetraploidy in mouse embryos.

Randomly bred Q strain mice kept under a natural diurnal light cycle were used throughout. Cleaving embryos were flushed from the oviducts of pregnant females 38–40 h *post coitum*. Most of these embryos are two-cell but a few three or four-cell embryos indicated that the second cleavage was imminent. It was therefore possible to allocate each cell to one of the following categories: (1) late G₂ or prophase (nucleus present); (2) division, either metaphase or anaphase (nucleus absent); (3) early G₁/S, with the cell dividing or divided. Although controversy exists as to the first appearance of the G₁ period in the mouse⁶ it is doubtful whether one exists at the four-cell stage⁷, even in slow-dividing strains⁸.

Groups of ten embryos were cultured in 0.1-ml drops of Whitten's medium⁹ under mineral oil in 60-mm plastic dishes. They were kept at 37° C and gassed with 10% CO₂ in air. Cytochalasin B (Imperial Chemicals Ltd) dissolved in dimethyl sulphoxide (1 mg ml⁻¹) was added to this medium to give a concentration of 10 μ g ml⁻¹. Tests had shown this to be the lowest concentration which would ensure complete inhibition of cytokinesis. Controls, grown with an equivalent amount of DMSO were run concurrently.

Embryos were put into cytochalasin for various periods of time. Many of the cells in G₂/prophase immediately show

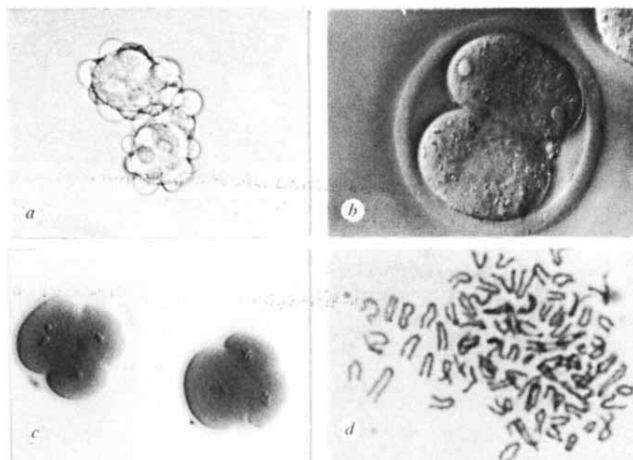


Fig. 1 *a*, A late G_2 two-cell embryo (with zona pellucida removed for clarity of illustration) showing extensive blistering of its cell surface after 7 min in $10 \mu\text{g ml}^{-1}$ cytochalasin B. *b*, A two-cell embryo with one blastomere binucleate and one with its nucleus in division after several hours in $10 \mu\text{g ml}^{-1}$ cytochalasin B. *c*, Two embryos recultured after becoming binucleate. One blastomere is still binucleate, one has a large metaphase plate (contributed to by two nuclei) and two blastomeres have already divided. These embryos were fixed with 3% glutaraldehyde before photography. *d*, A metaphase plate from the 12.5-d-old tetraploid embryo.

a vigorous cell membrane blistering (Fig. 1*a*). The blisters appear within 5 min and persist for some 10–15 min before the cell regains its normal smooth surface and shape. Some nucleated two-cell blastomeres do not blister and these have been found to be earlier in the G_2 phase than cells which do blister. These cells remain smooth and even when they approach and undergo mitosis show no indication of blisters.

Most cells in division remain smooth; exceptionally some late anaphase or telophase cells blister for about 10 min. Any cleavage furrow present recedes rapidly and disappears. Cleavage furrows fail to develop in cells which have not started cytokinesis. These observations are similar to those made on cleaving *Xenopus* and *Arhacia* eggs^{10,11} except that in those embryos the initiation of cleavage furrows is not prevented.

Cells in G_1/S show vigorous blistering (lasting 10–15 min) then revert to smooth surfaced cells. Cells at least 1 h into G_1/S do not blister but remain smooth and apparently unaffected by cytochalasin.

In those cells that are prevented from dividing by cytochalasin, the nuclei divide normally, at the correct time, giving rise to binucleate cells. The daughter nuclei then migrate to opposite poles of the cell where they come to lie very close to the cell surface (Fig. 1*b*). This process takes 2–4 h. Although there are reports of spontaneous enucleation of cells as a result of cytochalasin treatment^{1,12,13} this has never been observed in these mouse embryos.

Upon removal from cytochalasin and culture in fresh medium the binucleate cells behave differently depending upon their position in the cell cycle. If the nuclei are close together (corresponding to early G_1/S) when the cell is recultured, violent cell membrane blistering (lasting 10–15 min) occurs followed by the formation of several cleavage furrows. These furrows divide the cell into several pieces, two of which contain nuclei. These nucleated pieces will continue to develop normally, and form small but otherwise normal diploid blastocysts.

If the nuclei are at the poles of the cell when it is removed from cytochalasin then the cells remain in this condition until the next cleavage, which is a few hours delayed. Then, in about 60% of embryos, the nuclei move back into the cell centre and contribute to a single spindle (Fig. 1*c*). The cells divide, giving rise to a tetraploid four-cell embryo

which will continue to cleave and form a tetraploid blastocyst. These blastocysts contain a considerably reduced cell number (control, thirteen blastocysts; mean cell no. 49.9 ± 2.8 ; cytochalasin, sixty blastocysts, mean cell no. 19.1 ± 0.67). By selection of smooth surfaced two-cell embryos a few hours after removal from cytochalasin, which avoids those embryos which reverted to diploid and those where asynchrony has produced a diploid/tetraploid mosaic, it is possible to collect blastocysts which are uniformly tetraploid.

Some embryos fail to recover the ability to cleave after removal from cytochalasin although their nuclei continue dividing, each time contributing to a common spindle, and the cells become highly polyploid. In some twenty or thirty of these embryos I have encountered two two-cell “blastocysts” which were sixteen-ploid and a number of octaploid embryos.

From these observations a routine procedure was established for the production of tetraploid embryos, as follows. Two-cell embryos were put into cytochalasin between 1700 h and 1800 h on the second day of pregnancy and removed at 0600 h the following day. After this period no cell reverts to the diploid condition but 10–15% fail to cleave again. About 20–25% are somewhat delayed in their next cleavage. Usually about 40% of the initial two-cell embryos produce blastocysts but yields as high as 75% are possible.

Tetraploid blastocysts were transferred to the uteri of pseudopregnant foster mothers. Autopsies of the twenty-four recipient females examined so far showed that fourteen were pregnant and contained seventy-eight implantations from 112 blastocysts transferred. The majority of these implants (sixty-seven) showed that embryonic development was extremely limited and did not proceed into organogenesis (beyond 8.5 d). In similar experiments, Tarkowski and Witkowska (personal communication) have found that in tetraploid egg cylinders the formation of foetal membranes proceeds normally but the embryo itself does not develop. This syndrome is similar to that described for triploid mouse embryos¹⁴.

The remaining embryos in my experiments have shown development beyond the egg cylinder stage. Chromosome analysis has shown all to be tetraploid (Fig. 1*d*). Ten showed normal development up to the time of autopsy (including three live at term). The other, autopsied at 17.5 d, was abnormal. The ventral body wall of the embryo had failed to close and the viscera were externalized. The embryo was alive and showed no other gross abnormalities. This represents considerably greater development of tetraploids than has been achieved after cell fusion¹⁵ or other treatments¹⁶ in mammals.

Histological examination of several target sites in a 12.5-d tetraploid, compared with a similar stage diploid, indicates that the tetraploid is of normal dimensions but composed of fewer, larger cells. This suggests that the cell cycle time is not altered to any great extent by tetraploidy, at least up to 12.5 d of gestation.

It would seem from the results so far that there are not necessarily any developmental problems inherent in being tetraploid although death soon after implantation may sometimes be due to genetic imbalance (for example, aneuploidy, anomalies of X chromosome or sub-chromosomal inactivation). It is likely that the very low cell number in tetraploid blastocysts plays a significant part in reducing the developmental potential of the embryo^{17,18}. The technique of embryo aggregation^{19,20} is being used to investigate this parameter.

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Natural and Synthetic Sources of Circulating 25-Hydroxyvitamin D in Man

THE antiricketic sterols are both assimilated from the diet and endogenously produced by ultraviolet irradiation of cutaneous 7-dehydrocholesterol¹⁻³. Before the modern practice of supplementing foods with irradiated ergosterol (ergocalciferol, vitamin D₂), deficiency states were frequently observed in subjects whose dark skin colour and/or minimal exposure to sunlight minimized the natural endogenous production of cholecalciferol (vitamin D₃)⁴. It has been generally accepted that casual exposure to sunlight and average diets provide enough antiricketic sterol to prevent osteomalacia in the adult (American Academy of Pediatrics, 1963). Infants, however, are recognized to require vitamin D supplementation, for their maternally derived stores wane at a time when their natural foods are a poor source and their exposure to ultraviolet radiation unreliable. Supplementation of foods with vitamin D₂ has thus become a widespread and successful practice which has subsequently undergone quantitative revisions in several countries.

The minimum adult dietary requirement of vitamin D has been estimated to be 75 IU d⁻¹ in England⁵. Previous bioassay studies of human sera revealed increased antiricketic potency in subjects exposed to sunshine for most of the year⁶, and in persons fed large amounts of the synthetic vitamin D₂ (ref. 7). Precise quantification of the cutaneous contribution to body vitamin D stores has not been feasible to date but it has been observed that human exposure to ultraviolet radiation is followed by enhanced intestinal absorption of calcium⁸ and healing of vitamin D-deficiency states⁹. It is now recognized that vitamin D undergoes 25-hydroxylation in the liver¹⁰. The products, 25-hydroxyvitamins D₂ and D₃, are both known to be 150% more potent than the parent vitamin by bioassay^{11,12}. Subsequent 1-hydroxylation in the kidney produces an even more potent metabolite of the vitamin¹³ but the chief circulating form of the vitamin in man has been identified as the 25-hydroxy derivative¹⁴. Previous rat bioassay analyses of whole serum or serum extracts for antiricketic activity have, therefore, been non-

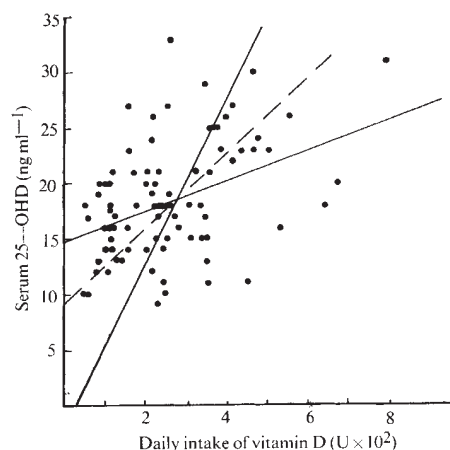


Fig. 1 Total serum 25-OHD concentrations as a function of estimated daily vitamin D ingestion by eighty-four Caucasian adults residing in St Louis, Missouri. —, Regression on each variable; ---, the "reduced major axis". $r=0.42$; $P<0.001$.

specific because the assay animals are capable of responding equally to vitamin D₂ or D₃, as well as to their 25-hydroxy and 1,25-dihydroxy derivatives.

While applying a radioligand assay for 25-hydroxyvitamin D (25-OHD)¹⁵ to human sera obtained randomly during the calendar year, we obtained diet histories quantifying average weekly vitamin D ingestion and estimates of time spent outdoors from eighty-four Caucasian adults (age range 16 to 70 yr) who had no evidence of disease or recent drug use. Their circulating 25-OHD levels, as a function of daily vitamin D ingestion, are shown in Fig. 1. The mean 25-OHD concentration for the group was 18.6 ± 5.2 (s.d.) ng ml⁻¹, and a significant ($P<0.001$) correlation between serum 25-OHD concentration and vitamin D intake was found. An ordinate intercept of 14.7 ng ml⁻¹ was observed. The "inverse" regression line and the "reduced major axis" are also shown¹⁶. The 95% limits of the intermediate intercept are -8.83 and 26.89 ng ml⁻¹ with a mean of 9.03 ng ml⁻¹. Thus, although the correlation between the two variables is significant, much of the variation in serum 25-OHD can be accounted for by factors other than vitamin intake. Also, the paucity of low intake values and data scatter prevented evaluation of a possible curvilinear relationship in which proportionately more of a smaller amount of the vitamin undergoes hydroxylation¹⁷. Plotting 25-OHD concentration against hours outdoors (<20 h per week in all cases) yielded a scattergram with no definite correlation. The estimates of time spent outdoors, however, were vague and often given in ranges, and were not indicative of other obvious variables such as clothing and weather. Our diet surveys indicated that some of the ingested vitamin D was in the form of D₃ but that the dominant source was the D₂ added to milk, cereals and multivitamin capsules.

We have previously shown that the radioligand assay cannot distinguish between 25-hydroxyergocalciferol (25-OHD₂) and 25-hydroxycholecalciferol (25-OHD₃)¹⁸. In order to examine directly whether or not the dominant circulating moiety of 25-OHD was indeed 25-OHD₃, we had to achieve chromatographic separation of 25-OHD₂ from 25-OHD₃. In this way we could establish whether the correlation observed in Fig. 1 reflected the partial influence of vitamin D₂ derived from diet on circulating 25-OHD. During the purification of ³H-25-OHD₂ produced by ricketic rats *in vivo*¹, we observed that the gradient silicic acid column¹⁹ fraction of ³H-25-OHD₂ eluted before ³H-25-OHD₃ on a standard calibrated LH-20 'Sephadex' column (65:35 chloroform/hexane)²⁰. ³H-Ergocalciferol, 1,200 d.p.m. per IU was administered to ricketic rats intraperitoneally, and blood was obtained 24 h later. By changing the solvent mix-

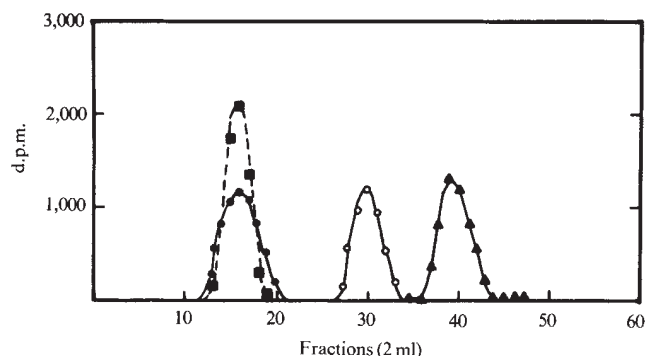


Fig. 2 Chromatographic profiles of radioactive ergocalciferol (D_2), cholecalciferol (D_3), 25-hydroxyergocalciferol (25-OHD₂) and 25-hydroxycholecalciferol (25-OHD₃) separately run on a calibrated 1 × 60 cm column of LH-20 'Sephadex' slurried in 50:50 chloroform/*n*-hexane. ▲, 25-OHD₃; ○, 25-OHD₂; ■, D_3 ; ●, D_2 .

ture to 50:50 and decreasing the volume of the collection fractions to 2 ml, the 25-hydroxy derivatives of vitamin D_2 and vitamin D_3 were separated (Fig. 2). As shown, the parent vitamins were not separated in this system. High specific activity 3H -(26,27)25-OHD₃ (19.7 Ci mmol⁻¹; Radiochemical Centre, Amersham) was used as a marker for the isolation of 25-OHD₃ from serum extracts by column chromatography.

Six normal adults were sampled between January and July, and the sera extracted as described previously²¹. Separate aliquots were subjected to the usual stepwise silicic acid column elutions¹⁵ or to chromatography on a 1.0 × 60 cm column of LH-20 'Sephadex' equilibrated in equal parts of chloroform and *n*-hexane. Recoveries were monitored by determining recovery of added radioactivity (tracer 3H -25-OHD₃) in the fractions obtained from the silicic acid and LH-20 'Sephadex' columns. Aliquots of the total 25-OHD (both 25-OHD₂ and 25-OHD₃) from silicic acid columns were measured in the radioligand assay. In the same assays, aliquots from those fractions of the LH-20 'Sephadex' columns marked by tracer 25-OHD₃ were also monitored. Thus, total 25-OHD and 25-OHD₃ concentrations were determined by assaying the silicic acid stepwise elution and LH-20 'Sephadex' fractions respectively.

As indicated in Table 1, most of the circulating 25-OHD in the sera from all six normal subjects was 25-OHD₃. Estimated dietary intakes of vitamin D were 150 to 350 U d⁻¹ and there was no history of inordinate sunlight or ultraviolet exposure in any of the subjects. Serum 25-OHD₃ averaged 84% of total serum 25-OHD content in this small group, supporting the influence of non-ingested sources indicated in the larger population survey (Fig. 1). Blood was obtained from two of the female subjects in late July, following several weeks of 25 to 35 h per week of sunbathing. As shown, the increases in total serum 25-OHD could be directly attributed to the increases in the 25-OHD₃ fractions (Table 1). A hypoparathyroid subject who had taken 50,000 U of vitamin D_2 per day for 6 yr was studied 4 months after the vitamin therapy had been discontinued. Analysis of this serum extract revealed only 18% (11 ng ml⁻¹) of the total 25-OHD to be 25-OHD₃, consistent with previous chronic ingestion of large amounts of D_2 . Also shown is the fractionation of serum 25-OHD observed in a young black male, one week after a subcutaneous injection of 3 mg each of vitamin D_2 and vitamin D_3 . Before therapy he had taken anticonvulsant drugs for many years and presented with hypocalcaemia and a total serum 25-OHD concentration of 0.3 ng ml⁻¹. The similar amounts of 25-OHD₂ and 25-OHD₃ in his serum 1 week after administration of D_2 and D_3 suggest comparable hepatic 25-hydroxylation of each form of the vitamin in this subject.

Our observations demonstrate that 25-OHD₃ is the dominant circulating moiety of 25-OHD in St Louis Caucasian

Table 1 Total Serum 25-OHD and 25-OHD₃ Concentrations in Various Subjects

Subjects	Race/sex	Month serum obtained	Total serum 25-OHD (ng ml ⁻¹)	% of total serum 25-OHD as 25-OHD ₃
Normal				
O. H.	C/M	February	16	90
R. W.	C/M	February	13	71
S. B.	C/M	February	24	91
M. M.	C/F	January	24	91
M. T.	C/F	January	21	83
M. T.	C/F	July	33	88
J. U.	C/F	January	25	82
J. U.	C/F	July	41	90
Hypoparathyroid				
E. M.	C/F	October	62	18
(50,000 IU vitamin D_2 d ⁻¹ stopped 4 months previously)				
Anticonvulsant Rx				
C. W.	B/M	September	12	46
(120,000 IU D_2 and 120,000 IU D_3 given 7 d before)				

adults and also indicate that ingestion and endogenous production of vitamin D_3 is the principal source of the vitamin in the population. Unless the diet is unusually rich in fish products, however, there are no important ingested sources of vitamin D_3 (ref. 22). Therefore, circulating 25-OHD₃ levels seem to reflect primarily endogenous D_3 production by the skin. Our results thus apparently represent the first direct quantification of the separate contributions of cutaneous production of D_3 and dietary ingestion of D_2 in man.

These conclusions, based on plasma levels of 25-OHD₂ and 25-OHD₃ carry the implicit assumption that D_2 and D_3 are metabolized in an identical manner^{11,12}. Vitamin D_2 and vitamin D_3 are generally considered equipotent in man but direct comparative examinations of their metabolism have not been performed. Although it is known that vitamin D_3 is stored in various tissues^{23,24}, factors affecting its assimilation, transport and release from storage sites are not well defined. Even less is known about the metabolic fate of D_2 . The dual application of radioligand assay and chromatographic techniques described here could be a most useful method for distinguishing synthetic and natural vitamin D sources and separately assessing their metabolic disposition.

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First Record of the Palaeocene Primate *Chiromyoides* from North America

PALAEOCENE fossil primates are known only from the European and North American continents. Fourteen genera and numerous species from North America have been described^{1,2}, and four genera (*Plesiadapis*, *Chiromyoides*, *Berruvius*, *Saxonella*) are recorded from Europe³. Only one primate genus, *Plesiadapis*, was previously known from the Palaeocene of both continents; the new species of *Chiromyoides* described below extends the range of this genus to North America. Addition of *Chiromyoides* brings to seven the number of mammalian genera known from the Palaeocene of both Europe and North America.

Stehlin⁴ gave the name *Chiromyoides campanicus* to a nearly complete left mandible from Cernay in France. Later additional specimens were found at Cernay, and at a nearby locality, Berru⁵. The morphology of the teeth of *C. campanicus* is similar to that of *Plesiadapis* and the two genera are classified together in the family Plesiadapidae. *Chiromyoides* differs from *Plesiadapis* in having a much deeper mandible and extraordinarily enlarged upper and lower incisors (Fig. 1). These incisors are the most diagnostic elements of its dentition. The short crown length compared with root length and relatively great anteroposterior diameter of the upper incisors, together with the dorsoventral expansion and robustness of the lower incisors, distinguish them from incisors of *Plesiadapis*.

Eleven incisors and the symphyseal region of a mandible of *Chiromyoides* have been found in collections from eight North

American Palaeocene localities (including the classic localities of Tiffany, Bear Creek, and the Clark Fork beds). The only complete incisor of *Chiromyoides* from North America represents a new species intermediate in morphology between the French species *C. campanicus* and early species of *Plesiadapis*.

Chiromyoides caesor, new species

Type: Princeton University Museum of Natural History No. 21575, a left upper central incisor collected by G. L. Jepsen from the early Late Palaeocene Croc Tooth Quarry, Section 5, T. 54 N., R. 95 W., Big Horn Co., Wyoming (see Fig. 2a and c and Table 1).

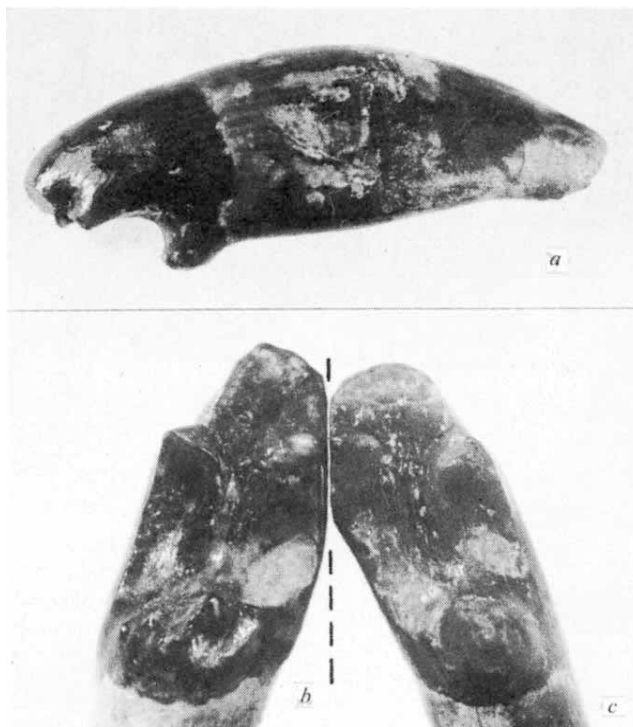


Fig. 2 Incisors of *Chiromyoides*. a, Type specimen of *C. caesor*, lateral view, $\times 4$; b, *C. campanicus*, occlusal view, $\times 7$; c, *C. caesor*, occlusal view, $\times 7$. — — —, Midline, note medial expansion of basal cusp of *C. campanicus*. Tip of *C. caesor* incisor is worn off.

Hypodigm: Type, and University of California Museum of Paleontology No. 36652, crown of a left upper central incisor collected by T. E. Reynolds from the Mason Pocket near Tiffany, Colorado.

Diagnosis: Same size as *C. campanicus* but differs from it in having a larger, more laterally positioned basal cusp, and in lacking medial expansion of the basal cusp to form a crushing platform (Fig. 2b and c). The specific name *caesor*, L., refers to the cutting function of the incisors, which distinguishes this species from *C. campanicus*.

The lower incisors of all species of *Plesiadapis* sheared against the large basal cusps of the upper incisors as they moved between them⁶. In *Chiromyoides campanicus* the basal cusps on the upper incisors were expanded medially to form a flat crushing area, and the function of the incisors was crushing rather than cutting. *C. caesor* is intermediate in having the enlarged incisors characteristic of *Chiromyoides*, while retaining cutting incisors typical of *Plesiadapis*. Incomplete incisors of *Chiromyoides* from the Clark Fork beds of Wyoming (probably representing more than one species) are morphologically more

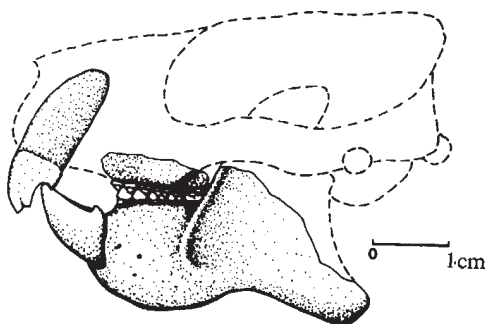


Fig. 1 Reconstruction of skull of *Chiromyoides campanicus*, based on materials described by Russell⁸ and Stehlin⁴. Compare with skull of *Plesiadapis*^{6,13}.

similar to *C. caesor* than to *C. campanicus*, suggesting that the crushing specialization of the incisors of *C. campanicus* may have been confined to a separate European lineage derived from a primitive form similar to *C. caesor*.

The newly discovered mandibular symphysis of *Chiromyoides* (P.U. 19125, from beds of Tiffanian age in Wyoming and provisionally referred to *C. caesor*) is of approximately the same size and morphology as that of *C. campanicus*. The fragment includes the root of the lower incisor and the roots of PM₃. Unfortunately the crowns of these two teeth are missing. The roots of PM₃ are somewhat larger than in *C. campanicus*, indicating that the cheek teeth of *C. caesor* were larger than those of the European species.

Table 1 Measurements of the Upper Central Incisors of *Chiromyoides caesor**

	Total length (mm)	Anteroposterior diameter (mm)	Transverse diameter (mm)
P.U. 21575 (type)	19.5	6.0	3.2
U.C.M.P. 36652	—	6.1	3.2

* Diameters measured at base of crown.

The presence of species of *Plesiadapis* and now *Chiromyoides* in both Europe and North America, and the close relationship of the European genus *Berruvius* to North American *Nava-jovius*⁹ and *Palenochtha*, indicate that the primate faunas of the two continents were probably very similar during late Palaeocene time. This is to be expected from the palaeontological and recent geophysical evidence of continental drift which suggests that Europe and North America were connected by Greenland throughout the Early Eocene⁶.

Martin⁷ and Cartmill⁸ have published broad comparative studies on the anatomy and behaviour of living primates, and discussed the definition and classification of primates. Both authors concluded that the fossils Plesiadapoidea⁹ (*Plesiadapis*, *Chiromyoides*, and their allies) differ so greatly from living Primates that they should not be classified in the same order. They did not, however, discuss the evidence on which allocation of these forms to Primates is based.

The first primates of modern aspect are found in deposits of Early Eocene age. The primitive adapid *Pelycodus*, and the primitive omomyids *Teilhardina* and *Tetonoides* seem to be stem primates close to the ancestry of the living lemurs and the tarsier, respectively. Comparison of the dentition of *Pelycodus*, *Teilhardina*, and *Tetonoides* shows them to have been closely related (which explains why the English adapid *Pelycodus eppsi* was considered for a time to be an omomyid¹⁰). Species of these three primitive primate genera share a number of morphological features which distinguish them from other Early Eocene mammals. The structure of the postprotocingulum ("nannopithec-fold") on the upper molars, and the relationship of trigonid cusps, together with broad talonids on the lower molars, are characteristic of the Early Eocene primate species. These features are not found in known Late Cretaceous mammals and seem to be good synapomorphic characters of primates, that is, specific characters acquired after separation of the primitive primate stock¹¹. The living *Tarsius* has primitive lower molars of the *Pelycodus-Teilhardina-Tetonoides* pattern, the most uniform modification being the development of a hypocone from the primitive postprotocingulum.

The dental characteristics distinguishing primitive Early Eocene adapids and omomyids from other Eocene mammals are present in primitive plesiadapoids, and also distinguish them from other Palaeocene mammals. Thus, the most logical place to look for the common ancestor of *Pelycodus*, *Teilhardina*, and *Tetonoides* is among the Palaeocene Plesiadapoidea. The molars of Palaeocene plesiadapoids are more similar to the molars of these Early Eocene primates than to those of any other group

of mammals. It is unlikely that this is a result of evolutionary convergence considering the detailed nature of the resemblance and the fact that the Palaeocene plesiadapoids immediately precede the early Eocene primates in time. If primate classification is to represent probable primate phylogeny, the Plesiadapoidea are most reasonably classified as a primitive suborder of Primates. Removal of plesiadapoids to Insectivora, as Cartmill⁸ proposed, would simplify the diagnosis of Primates, but this diagnostic simplification certainly would not justify the resulting loss of phylogenetic information.

The best known Palaeocene primates (*Plesiadapis*, *Phenacolemur*, *Palaeochthon* and *Plesiolestes*¹²) gave rise to now extinct side-lines of early primate evolution, but some of the smaller forms (*Palenochtha*, *Berruvius*) are still poorly known anatomically and may prove to be close to the ancestry of adapids and omomyids. Recent addition of the genus *Torrejonius*², and now *Chiromyoides*, to an already large North American fauna of Palaeocene primates suggests that the fauna is still not completely known. The ancestral adapid-omomyid may yet be discovered in the Palaeocene European-North American faunal province.

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Amphibious Nature of Visual Acuity in the Asian "Clawless" Otter

THE ability to acquire information at some distance and to behave accordingly increases the probability of species survival and reproduction. The propagation of light and sound differs to such a great extent in air as compared with underwater that special sensory adaptations are necessary for an animal to operate effectively in both media.

Recently there has been great interest in the amphibious nature of visual and auditory acuity in a variety of aquatic animals, including turtles¹, river otters², sea otters³, mink⁴, porpoises⁵, pinnipeds⁶ and man^{7,8}. The latter, for example, shows an expected 20 dB hearing loss under water⁷; also when not wearing goggles the loss of refractive power of the cornea under water⁹ cannot be sufficiently compensated by the accommodative power of the lens so that, at a distance of 0.7 m, human visual acuity in water suffers an eight-fold decrease compared with that in air, and at a distance of 5 m

humans are virtually unable to resolve sufficient detail to differentiate form from background⁸. Thus man, like other terrestrial mammals that have not developed special adaptations for seeing under water, is hypermetropic in water while being emmetropic in air. On the other hand, truly amphibious mammals like the pinnipeds, which feed exclusively under water and carry out many reproductive functions on land, have essentially an emmetropic eye under water while possessing special dioptric mechanisms for seeing detail in air.

Pinnipeds have developed a permanently changed curvature of the lens for seeing under water. On the other hand, otters are thought to have a similar device to turtles, in having well developed ciliary and sphincter muscles which squeeze the anterior part of the air adapted lens, giving it a focal length similar to that of a spherical lens⁸.

The visual acuity of the Asian "clawless" otter has been measured both in air and under water under a light intensity level of 100–200 m^l (ref. 2), and it was found that the closest grating spacings that could be resolved in both media subtended visual angles ranging from 14–16 arc min. As this special adaptation of otter underwater vision is thought to be achieved primarily by the action of the powerful iris sphincter closing down on and distorting the lens, a question arises as to the effects of ambient light on the iris sphincter. If the pupil fully dilates under low light levels, then the lens would not become sufficiently spherical, thus resulting in the otter's eye becoming hypermetropic in water. This would in turn lead to the hypothesis that as luminance decreased under water, visual acuity in otters would deteriorate at a more rapid rate under water than it would in air. To test this, we measured the aerial and underwater visual acuity of two mature male Asian "clawless" otters (*Amblonyx cinerea cinerea*) in three ambient light conditions.

The testing tank apparatus, general testing procedures and acuity targets were the same as those used previously². Acuity targets were produced from 12.7² cm photos of Ronchi rulings with black and white stripes of equal width. The standard grating consisted of 300 lines per inch, the variable gratings of lines varying in width from 12.7 mm to 4.8 mm. Targets were presented simultaneously by lowering a target board from behind an opaque screen. The only modifications were to control ambient light intensities, simply by covering the top of the apparatus with a double layer of 8 mill black vinyl sheeting. The amount of light entering the tank and reflected from the targets was controlled by opening the top cover a given amount. At the start of each test session the experimenter dark adapted and an assistant would then slide back the black vinyl cover until the desired light level was obtained. The light intensities were 0.3, 0.03 and 0.009 m^l. Daily light readings were taken with an SEI meter which was checked against a Macbeth illuminometer.

The otters were maintained at fixed distances of 1.7 m and 1.3 m at the highest light level, 1.3 m at the next highest light level and at 0.76 m at the lowest light intensity. A modified psychophysical method of limits was used to obtain visual acuity thresholds.

In most conditions each animal's threshold was defined as the interpolated values at which the animal responded correctly 75% of the time. If an otter never achieved a value of 75% correct responses or better, however, then the threshold was defined in terms of visual acuity targets resulting in discrimination performance which was significantly better than chance ($P < 0.01$).

At each test session ambient light levels remained relatively constant, and stripes were made finer if the animal succeeded in making seven or more correct responses in ten successive trials. The otters were dark adapted 30 min before each test session.

The main results of the experiment (Table 1) clearly support the idea that visual acuity in otters, although showing an air-water equivalence in relatively bright light, degrades at a considerably more rapid rate in water than in

air. The lack of visual accommodation in otters under water in the dark may be due to pupillary dilation resulting in insufficient squeezing of the anterior portion of the lens by the iris sphincter muscles. On the other hand, one might argue that the present findings are not due to the lack of lens accommodation, but result from insufficient pupillary dilation in the dark, thus reducing the amount of light entering the submerged eye. This explanation assumes that squeezing of the lens by the pupil aperture occurs either voluntarily or is triggered reflexively soon after the otter goes under water.

Table 1 Aerial and Underwater Visual Acuity Thresholds* as a Function of Ambient Light Levels

Luminance (m ^l)	River otter, Tom Air	River otter, Tom Water	River otter, Jerry Air	River otter, Jerry Water
100–200†	14	15	15	16
0.3	18	18	17	17
0.03	23	33	23	33
0.009	39	57	38	58

* In minutes of visual angle.

† Data from Balliet and Schusterman².

It is interesting to compare the present experiments with otters whose eye is emmetropic in air with special adaptation for seeing under water, with similar experiments using seals and sea lions whose eyes are emmetropic under water with special adaptations for seeing in air.

In the California sea lion (*Zalophus californianus*) aerial acuity deteriorated at a much more rapid rate than underwater acuity in the luminance range of 3 to 0.000003 m^l (ref. 6). These results are consistent with the idea that as pupil size in seals and sea lions varies with ambient light intensity regardless of whether the eye is submerged¹⁰, the narrow vertical slit pupil in air provides good visual acuity in relatively brighter light, but in dim light the pupil is dilated and aerial visual acuity is reduced by the astigmatism of the cornea. Although the pupil is dilated under water, the corneal astigmatism of sea lions plays virtually no role because of the similar refractive indices of the cornea and water.

Thus a comparison of the effectiveness of the visual systems of modern aquatic mammals suggests that only when tested under a wide range of lighting conditions is there a correlation between the degree of adaptedness of different amphibious species to aquatic and terrestrial habitats.

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Changes in Fishing Ability of Terns associated with Windspeed and Sea Surface Conditions

THE terns are a group of largely marine fish-feeders, many of which obtain their prey by skilful air-to-water plunge diving. Previous observers have assumed that light winds and rippling of the water surface either have no effect¹ on the fishing success of terns or else are detrimental², but there has been no direct evidence to support either view. To investigate this problem, a study of Sandwich terns (*Sterna sandvicensis*) and common terns (*Sterna hirundo*) was carried out in Northumberland, England.

Both species were easily observed as they foraged close inshore, diving from heights of 3–10 m. The tern, if successful, emerged from the water with its prey held conspicuously in its bill. Daily fishing success (percentage of plunge dives yielding prey) was derived from several hours' observations involving many different birds. Plunge diving rates were obtained by timing individual bouts of feeding activity (for 2–10 min). The sea surface conditions encountered in the foraging area were classified by presence or absence of ruffling as either "calm" (=surface smooth or slightly rippled ± light swell) or "moderate" (=windchop ± light swell). Windspeeds (in knots; 1 knot = 1.85 km h⁻¹) were obtained from a meteorological station situated 4.8 km inland from the main study area.

So as to eliminate the known effects of tidal movements^{3,4} fishing ability is compared over an equivalent part of the tidal cycle on different days. In 1968 and 1969 the fishing success of both species was better in moderate than in calm seas (Table 1). Although overall success was appreciably higher in 1969, the proportional improvement from calm to moderate conditions was similar for both species in the two years. Furthermore, the fishing success of the two terns was directly correlated on a day-to-day basis ($P < 0.02$). A comparison of capture rates (Table 2) takes account of the birds' tendency to dive at a faster rate in moderate than in calm seas.

Table 1 Mean Daily Fishing Success (± 1 s.e.) in Calm and Moderate Sea Conditions

	Calm			Moderate		
	Success (%)	Days	Dives	Success (%)	Days	Dives
Sandwich tern						
1968	11.0 $\pm$ 1.5	5	504	16.8 $\pm$ 1.5	6	535*
1969	35.7 $\pm$ 1.5	4	411	57.5 $\pm$ 5.5	4	362†
Common tern						
1968	17.0 $\pm$ 4.4	4	265	27.9 $\pm$ 5.4	3	212 n.s.
1969	21.9 $\pm$ 2.6	4	156	38.9 $\pm$ 6.0	4	191*

* = P success < 0.05 . † = P success < 0.01 . n.s. = P success not significant.

For Sandwich terns both fishing success and capture rates (Fig. 1a) were directly correlated with windspeed ($P = 0.02$, $P < 0.02$ respectively) whereas plunge diving rate was not. These correlations raise the problem of distinguishing the effects of wind *per se* from those of related surface conditions. The extent of surface disturbance is not, however, directly related to prevailing windspeeds. A choppy sea, for example, persists after the wind responsible has abated. Again, an onshore breeze may produce a moderate sea inshore, whereas a calm sea may occur with an offshore breeze of the same strength. Such effects allowed a comparison of capture rates in a variety of windspeeds with differing surface conditions for each. For any particular windspeed, moderate conditions were generally associated with a higher

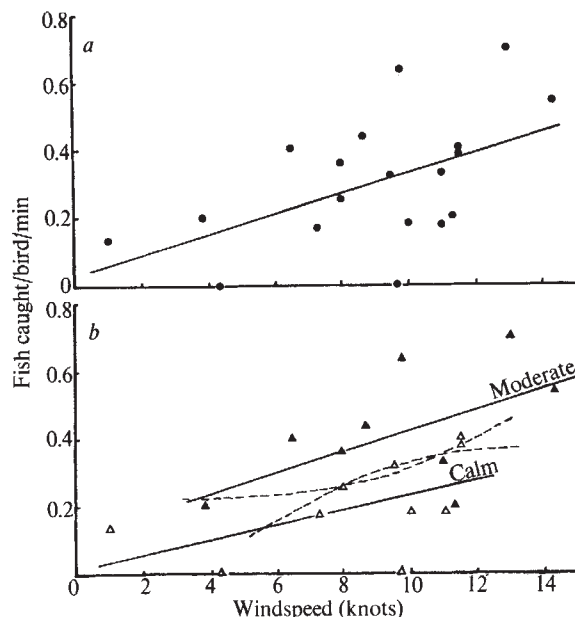


Fig. 1 Prey capture rates of Sandwich terns in different windspeeds. In (a) no distinction is made for sea conditions and a single regression line ($y = 0.03x + 0.03$) is shown ($P < 0.02$). In (b) separate regressions are calculated for calm (Δ) ($y = 0.02x + 0.01$) and moderate ($\blacktriangle$) ($y = 0.03x + 0.11$) sea conditions. The 95% confidence limits are shown by the broken lines.

capture rate than calm conditions (Fig. 1b). Although neither the "calm" nor the "moderate" regression is significant, they are approximately parallel and their 95% confidence limits differ in elevation between 8–11 knots. This suggests that surface conditions may contribute independently of windspeed to influence fish capture rates of Sandwich terns. None of these differences in fishing ability was correlated with variation in cloud cover.

Table 2 Mean Daily Rates of Prey Capture (± 1 s.e.) in Calm and Moderate Sea Conditions

	Calm		Moderate	
	Prey min ⁻¹	Prey h ⁻¹	Prey min ⁻¹	Prey h ⁻¹
Sandwich tern				
1968	0.10 $\pm$ 0.04	6	0.29 $\pm$ 0.04	18†
1969	0.32 $\pm$ 0.05	19	0.73 $\pm$ 0.11	44*
Common tern				
1969	0.23 $\pm$ 0.02	14	0.50 $\pm$ 0.08	30*

* = P prey min⁻¹ < 0.05 . † = P prey min⁻¹ < 0.01 . Prey h⁻¹ are extrapolations assuming sustained foraging activity. No common terns were timed in 1968.

Various authors¹⁻⁶ have noted that in stormy conditions terns experience difficulty in obtaining food, probably because it is hard to maintain an accurate diving trajectory and because fish may remain further below the surface. It has not previously been realized, however, that within a certain range, increasing windspeed produces conditions which facilitate fish capture. I suggest therefore that these conditions reach levels that optimize fishing ability after which their effects are increasingly detrimental to the birds. It only remains to explain the initial improvement in fishing ability. First, most plunge dives are preceded by hovering and it appeared that the less wind there was, the more vigorously did terns have to hover in order to remain stationary. Fish can probably detect and respond to move-

ment of terns hovering a few metres above the surface⁷. Prey may therefore have a better chance of spotting terns on still days which demand concerted hovering effort. Second, the fish caught are much closer to the water surface than the tern and it is probable that with increasing disturbance the surface acts rather like a sheet of frosted glass to impair the fish's view of the tern much more than the tern's view of the fish.

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Mitosis in the Cryptophyceae

RECENTLY a number of papers have been published describing the fine structure of nuclear division in the algae. This interest has no doubt been stimulated by the great variety of nuclear structures found and their relevance to current discussions on algal phylogeny¹⁻³. In the past year we have had the first detailed accounts of mitosis in the Chrysophyceae⁴, Xanthophyceae⁵, Chloromonadophyceae⁶, Rhodophyceae⁷, and Phaeophyceae⁸. This leaves only three classes, Prasinophyceae, Eustigmatophyceae and Cryptophyceae in which details of mitosis are unrecorded. We would like to help complete the picture of algal division by making known some recent findings about mitosis in a member of the Cryptophyceae, *Chroomonas salina* (Wislouch) Butcher.

Mitosis in *Chroomonas* is characterized by the following features. (1) Before the start of mitosis the flagellar bases divide. Microtubules extend from the flagellar bases to the area of cytoplasm around the nucleus. These seem to be randomly arranged and are often very close to, or in contact with, the nuclear envelope. (2) As the nuclear envelope breaks down the microtubules extend into the nucleus. The chromatin aggregates into a pear shaped mass through which pass tunnels free of chromatin. This is interpreted as a part of prophase. (3) The nuclear envelope breaks down but areas of nuclear envelope material may remain. The extent and positioning of this material are variable. The area in which mitosis occurs is roughly delimited by sheets of endoplasmic reticulum. (4) At metaphase the chromatin is aggregated into a dense plate on the equator (Fig. 1a). Many spindle microtubules pass through channels in this plate and others seem to connect with the chromatin mass. No kinetochores were seen. (5) No centrioles or spindle organizing bodies appear to be present though microtubules can occasionally be seen to contact the endoplasmic reticulum surrounding the mitotic area. No connexion was seen between the flagellar bases and the spindle microtubules at metaphase or anaphase. (6) At anaphase two dense clumps of chromatin separate. Individual chromosomes cannot be distinguished in these clumps (Fig. 1b). (7) In telophase the chromosome clumps appear to be pushed back into the endo-

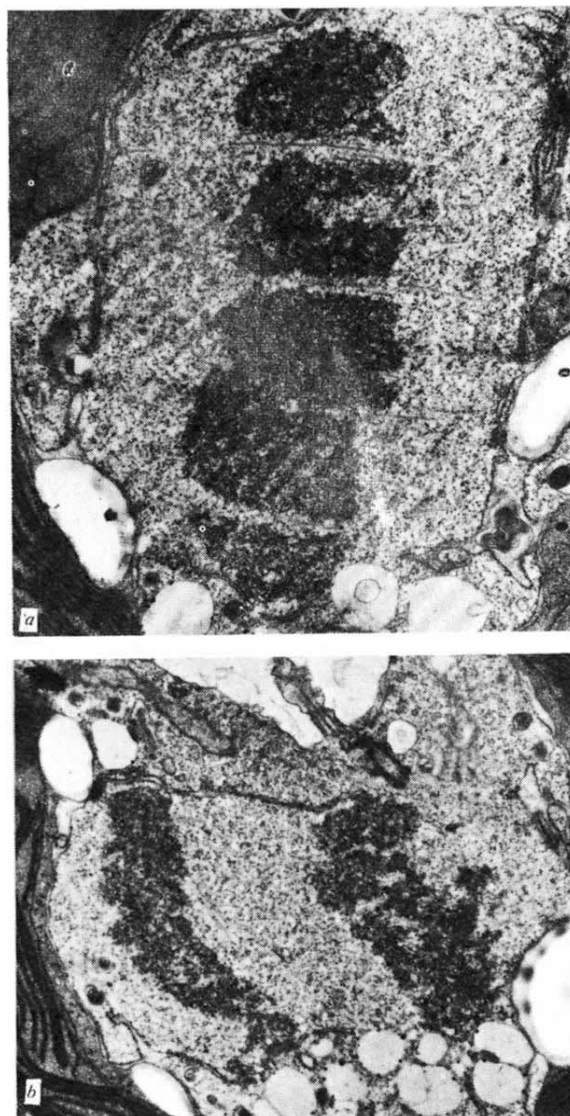


Fig. 1 *a*, A section through a metaphase of *Chroomonas* showing the chromatin aggregated into a dense plate on the equator. A number of the spindle microtubules can be seen to pass through channels in the plate. $\times 17,000$. *b*, A similarly orientated section through an anaphase of *Chroomonas* showing the chromatin separating in two dense masses. Individual chromosomes cannot be distinguished. $\times 9,350$.

plasmic reticulum sheath surrounding the chloroplasts and this appears to form the first part of the nuclear envelope. New nuclear envelope material seems to be formed on the opposite side of the nucleus.

Early light microscopic work on another cryptophyte, *Chilomonas paramecium*, suggested that true chromosomes did not exist⁹⁻¹¹. Later microscopical work reported, however, that this organism possessed many very small chromosomes¹². Our work suggests that on an ultrastructural level, multiple chromosomes cannot be distinguished, though the tunnels through the metaphase plate might give the impression that there were many distinct chromosomes if a section through only one plane was examined, or possibly if the nucleus was squashed before examination. It would be very interesting to see if the chromatin behaves genetically as one chromosome pair.

This form of mitosis is clearly distinct from that of the Dinophyceae¹³, to which the Cryptophyceae were thought to be closely related. It is also quite different from that of the

Rhodophyceae⁷ which has certain similarities of pigmentation. It appears to resemble most closely the mitosis of *Prymnesium* (Haptophyceae)¹⁴ and to have some similarities with that of *Ochromonas* (Chrysophyceae)⁴. In the endosymbiotic scheme for the origin of plastids and phylogeny of algae proposed by Lee¹⁵, the Cryptophyceae were thought to be ancestral and closely related to the Cyanophyceae. Our findings show no evidence, however, for a primitive condition in nuclear or mitotic structure. It would seem possible that the mitotic process may give quite a different phylogenetic picture from that obtained with chloroplast structure and pigmentation.

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Linguistic Structure and Speech Shadowing at Very Short Latencies

SPEECH shadowing is an experimental task in which the subject is required to repeat (shadow) speech as he hears it. When the shadower is presented with a sentence, he will start to repeat it before he has heard all of it. The response latency to each word of a sentence can therefore be measured.

The response latencies reported^{1,2} for the accurate shadowing of continuous prose typically range between 500 and 1,500 ms. These latencies may be compared with those obtained in reaction-time (RT) experiments in which the subject repeats isolated words or nonsense syllables. In such studies³⁻⁷, the RT's are of the order of 150 to 250 ms. This difference in RT's may seem to reflect differences in complexity between sentences and lists of isolated items for, according to modern psycholinguistic theory, higher order linguistic structure plays an essential role in the process of speech perception. Such higher order structure (syntactic and semantic) is defined over units of analysis at least as large as a phrase. Thus, to use this information, the shadower would not be able to respond until he had heard at least a phrase, and should therefore have longer repetition latencies to prose material than to unstructured lists.

This report establishes that it is possible, however, to shadow continuous prose accurately at latencies as short as those found for isolated items, and examines the question of such shadowers' use of higher order linguistic structure.

Sixty-five subjects were screened in a search for individuals who could shadow closely while still repeating the material clearly. Seven of these proved capable of shadowing at mean delays of 350 ms or less while still maintaining the intelligibility of their speech. All the other subjects were only able to shadow clearly at rather longer latencies (500–800 ms).

The seven close shadowers, together with seven of the more distant shadowers, then shadowed a pair of 300-word passages of normal prose read at a normal conversational speaking rate (160 w.p.m.)⁸. The passages were presented binaurally through headphones. The subjects' production was recorded onto one track of a tape-recorder, while the material they were hearing was simultaneously recorded on a second track. For each passage, the repetition latency was measured from a polygraph tracing of the two records, always at the beginning of an easily identifiable word. The seventy-five measurement points were distributed equally over the passage at different serial positions within sentences, and were the same for all subjects.

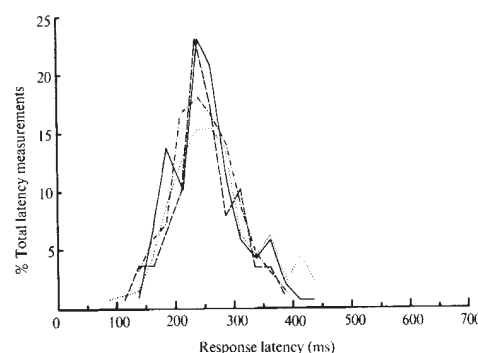


Fig. 1 The distribution of latencies for four very close shadowers.

Of the seven close shadowers, the response latencies of the four closest are plotted in Fig. 1. The mean latencies of these four shadowers ranged between 254 and 287 ms, with standard deviations of between 54 and 85 ms. Their error rates ranged from 1.7 to 6.6%.

In comparison, the responses of two of the less close shadowers and of two of the distant shadowers are plotted in Fig. 2. These curves are typical of those found for subjects not shadowing consistently at very short latencies. The mean latencies for these subjects were 305, 362, 559 and 600 ms respectively. The standard deviations ranged between 85 and 129 ms, with error rates of 0.5 to 5.8%.

The mean syllable duration for material read at a rate of 158 w.p.m. is 200 ms (ref. 9). Thus, to shadow at a distance of 250 ms is to remain little more than a syllable behind the original material. We know that it is possible to repeat isolated syllables with similar or even shorter delays. This suggests that the closest shadowers are processing the incoming material at the level of individual syllables. Such a mode of speech analysis needs to be reconciled with the recent psycholinguistic emphasis on the importance of syntactic and semantic structure in speech perception.

If the close shadower is not using syntactic and/or semantic structure, then he should not have available to him information that could only derive from these levels of analysis. One way of testing this is to question the subject about the content of a passage he has shadowed. Thirteen of the fourteen subjects were given a further passage to shadow, 600 words long and again presented at 160 w.p.m. They were not told in advance that they would be given a memory test. Immediately following the passage, they were asked a series of questions about it. The results showed very little relation between latency and memory for content. There was a small, nonsignificant, negative correlation ($r=0.18$) between increasing latency and

memory score. No difference was found between the scores of the shadowers and a control group of listeners.

The results of the memory test show that syntactic/semantic information is available to the shadower irrespective of his shadowing latency, but this does not exclude the possibility that the shadower performs the higher level analysis of the material after he shadows it. The close shadowers could produce their output on the basis of a low level analysis and perform the rest of the analysis later. Such a procedure should be reflected in the subjects' errors.

If the shadower's performance is based, for example, on a syllabic analysis of the material, then his errors should be constrained by the syllabic character of the material, but not by its semantic or syntactic character. Furthermore, if the relative distance of an individual's shadowing performance is a function of the "depth" to which he analyses the material, then there should be latency-dependent differences in the types of errors which the subjects make.

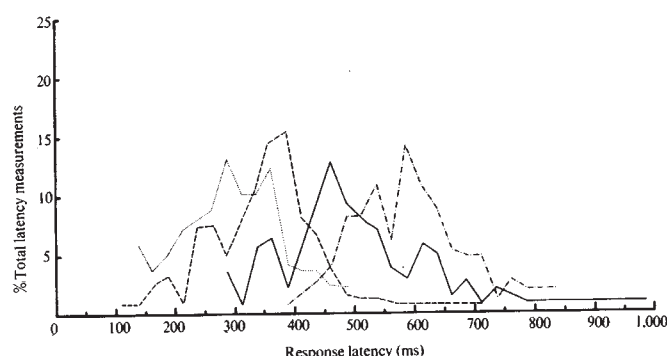


Fig. 2 The distribution of latencies for four subjects shadowing at distances greater than 300 msec.

The errors made on the two passages of normal prose were therefore analysed. Of the total of 402 errors made by the fourteen subjects, 221 were delivery errors (slurring, hesitations, etc.), 49 were omission errors, and 132 were constructive errors in which subjects either added or changed entire words, or changed part of a word so as to make it into a different word. Twenty-one of the latter resulted in syntactically/semantically unanalysable nonsense words.

The remaining 111 constructive errors were analysed according to their grammatical suitability with respect to the preceding context. Of these, only three were structurally inappropriate. All the other errors were both semantically and syntactically congruent with the preceding context. A regression analysis showed there to be no systematic relationship between shadowing latency and grammaticality of errors. Although the closer subjects tended to make more errors overall ($t=2.403$ (d.f. = 13), $P<0.025$), this difference derived more from the delivery errors ($t=2.308$ (d.f. = 13), $P<0.025$) than from the constructive errors ($t=1.411$ (d.f. = 13), $P<0.10$). Indeed, if each subject's total grammatical errors are expressed as a proportion of his total errors, then one finds no latency-dependent differences at all ($t=0.248$ (d.f. = 13), $P<0.50$). These results are not consistent with the idea that higher order structure is not available at very short latencies.

The constructive errors of close and distant shadowers are also qualitatively very similar, and indeed the same errors were sometimes made by subjects in both groups. For example, in the sentence "It was beginning to be light enough so I could see . . .", two subjects inserted the deleted "that" following "so": one shadowing at 254 ms, the other at 559 ms. In the sentence beginning "He had heard at the brigade . . .", five subjects replaced "heard at" with "heard that": their latencies were 264, 287, 362, 444, and 553 ms. Nor do these errors

occur only when the subject's shadowing delay is longer than usual. These errors, especially in the case of the closest shadowers, usually occur when the subjects' latencies are shorter than average, as if they are placing more reliance on the predictive properties of the higher order context.

These examples, and the errors in general, also show that the subjects' output can be constrained by the preceding context up to and including the word immediately before the error. The error "that" in the first example is clearly contingent on knowing that the preceding word is "so". Similarly, in the second example, the subjects would need to have extracted the structural implications of "heard" to make the grammatically appropriate error of saying "that" instead of "at".

There seems to be no difference between close and distant shadowers in their use of the semantic and syntactic information available. The data suggest that all the subjects analyse the material up to a semantic level as they repeat it, and that this analysis helps to determine the ongoing series of perceptual decisions underlying their shadowing performance. The significance, therefore, of very close shadowing is not that it indicates some anomalous minimal mode of speech processing, but that it seems congruent with what we know of normal speech perceptual processes. The present results, in these terms, pose problems for any theory of speech perception which requires that the assignment of higher order structural descriptions await the end of a major constituent.

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Axenic Culture of a Plant Pathogenic Spiroplasma

EVIDENCE has accumulated that a number of insect-transmitted plant diseases of the "yellows" group result from the infection of plants by organisms resembling mycoplasmas^{1,2}. Circumstantial evidence suggests that two such diseases, corn stunt and citrus stubborn, may be caused by a novel type of helical prokaryotic microorganism lacking a cell wall, for which the trivial name "spiroplasma" has been proposed³. The agent of corn stunt has so far defied attempts at culture in a cell-free medium and although an organism associated with citrus stubborn disease has been successfully cultured from diseased

plants^{4,5} it has not, to our knowledge, been shown to be a plant pathogen.

Citrus little-leaf, a similar disease to citrus stubborn, was first observed in Palestine in 1928⁶. No insect vector has yet been identified. Zelcer *et al.*⁷ have observed mycoplasma-like organisms in electron micrographs of ultrathin sections of infected plants.

"Lop-sided" fruits from sweet orange trees (*Citrus sinensis* cv. Valencia) with little-leaf disease were washed and surface-sterilized with 70% (v/v) alcohol. The aborted seeds were then removed aseptically and rinsed in sterile water. Seed coats were selected for study because it is known that the citrus stubborn agent may be cultured from this tissue⁸. They were ground with sand in the growth medium of Saglio *et al.*⁵, containing the selective agents 'Floaxapen' (Beecham) 50 µg ml⁻¹ and, in later experiments, thallos acetate (0.05%, w/v). The extracts were then centrifuged at 500g for 2 min to remove debris and filtered through sterile 'Millipore' membrane filters (0.45 µm pore diameter). The filtrate was diluted with further growth medium and incubated at 32° C. Portions were also streaked and incubated on plates of medium solidified with 1% 'Ionagar' No. 2 (Oxoid).

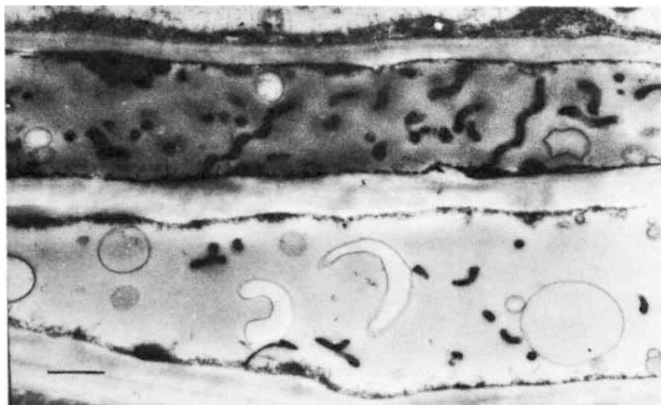


Fig. 1 Electron micrograph of a section (about 150 nm thick) of phloem in a petiole from an infected clover plant showing spiroplasmas in sieve tubes. The scale bar represents 1 µm.

After 7–10 d, slight turbidity was noted in the liquid cultures and acid production was shown by a change in colour of the phenol red internal indicator from red to yellow. Examination by phase-contrast microscopy revealed large numbers of delicate helical filaments about 0.2 µm in width and up to 15 µm long, exhibiting the type of whirling and flexing movement described by Davis and Worley³ for the corn stunt spiroplasma. Small colonies (about 0.1 mm diameter) having the "fried egg" appearance typical of mycoplasma colonies were observed on plates. Electron micrographs of thin sections of colonies and of organisms centrifuged from broth cultures showed that the filaments were bounded only by a unit membrane, no traces of external cell wall material being seen. Their appearance was identical with that of the organisms shown in Fig. 1. We found no reversion to walled forms when the spiroplasmas were grown in the absence of penicillins.

We received seven batches of fruit showing symptoms from separate trees and were able to culture spiroplasmas from all of them. In contrast, no isolations were achieved from a number of samples of healthy fruit from several sources. Heating the seed coat extract to 40° C for 20 min, before dilution with further growth medium, completely prevented growth of the spiroplasmas.

After serial subculture equivalent to a dilution of the original diseased plant extract by a factor of at least 10²⁵, broth suspensions of spiroplasmas were injected into leafhoppers (*Euscelis plebejus* (Fallén)) known to act as vectors of some European yellows type diseases. The insects were caged in groups of forty on white clover plants (*Trifolium repens* L. var. S100) at 25–30° C. After about 5 weeks four out of seven test plants developed severe symptoms of chlorosis followed by stunting and dwarfing of young leaves. No such symptoms were observed on a large number of control plants maintained insect-free, or on those exposed to insects which were either uninoculated or injected with sterile broth. Electron microscopy demonstrated the presence of many spiroplasmas in phloem tissue of the infected plants (Fig. 1), but not in healthy plants. We were able to culture spiroplasmas from the insects for at least 10 weeks after injection, and we reisolated the organisms from the infected clover plants. The pathogenicity tests were repeated, with similar results, using further spiroplasma subcultures.

Our experiments have demonstrated the association of spiroplasmas with the plant disease, citrus little-leaf. We have cultured the microorganisms and by using an insect as a vector we have been able to show for the first time that spiroplasmas are plant pathogens. We are at present attempting to transmit the organisms to citrus plants in order to fulfil Koch's postulates and prove, as seems highly probable, that spiroplasmas are the aetiological agents of citrus little-leaf.

We thank Dr B. Raccach, of the Volcani Centre, Agricultural Research Organization, Israel, who provided the "lop-sided" fruits of *Citrus sinensis*. M. B.-J. is a visiting worker from the Volcani Centre and acknowledges a fellowship awarded by the Royal Society.

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Reference Abbreviations

FROM September 1 it is *Nature's* intention that all abbreviations of references should conform to the style of the *World List of Scientific Periodicals*, fourth ed. (Butterworth, 1963–65). The changeover will be gradual and authors submitting manuscripts from now on are asked to ensure that the references are written appropriately.

BOOK REVIEWS

Hoyle on Copernicus

Nicolaus Copernicus: An Essay on his Life and Work. By Fred Hoyle. Pp. vii+94+6 plates. (Heinemann Educational: London, May 1973.) £1.50.

NEARLY everyone is ready to honour Copernicus, yet very few can explain exactly what he achieved. "His heliocentric picture of the solar system was the beginning of modern science" is the kind of cliché that hides several half-truths. The heliocentric picture was propounded by Aristarchus of Samos nearly 1,800 years earlier: does Copernicus deserve much credit for merely reviving it? Paradoxically he does, because he had to face a greater obstacle than Aristarchus, namely the entrenched dogma in favour of the geocentric theory, built up over many centuries. But even in ancient times the idea of planets elegantly circling the Sun was abandoned because it did not fit the facts well enough, and Ptolemy's inelegant but effective system of epicycles came to prevail. The achievement of Copernicus was to devise a heliocentric system that described the planetary motions as well as Ptolemy's (or almost as well), yet also held the potential for fruitful mathematical development in the hands of Kepler and Newton.

Fred Hoyle has now written an admirable little book clearly explaining the achievements of Copernicus for anyone who is prepared to follow some straightforward equations. The main difficulty in writing about Copernicus is to make a detailed comparison with Ptolemy, and Hoyle does so by expressing the radius vector of a planet as a complex number, expanding in powers of the orbital eccentricity e and (generally) neglecting terms in e^2 . Interpreted geometrically, the results show clearly the similarities and differences between the Copernican and Ptolemaic systems, but without the elaborate constructions which so often baffle modern readers. (Incidentally, Ptolemy comes out of the comparison very well.) Although this is the crux of the book, the earlier chapters usefully prepare the way by describing the Aristarchan heliocentric system. In addition there is a 23-page biographical chapter—not

just a re-hash of the standard biographies of Copernicus, but a fresh look. In Hoyle's view, the idea that the Earth rotated was accepted by Copernicus before he was 30, but he only began serious quantitative work on the solar system when he was 40, and the theory was fully developed in his fifties, between 1523 and 1533.

The book is attractively written and animated by a light personal touch, to remind us that

True ease in writing comes from art,
not chance,

—in this instance the novelist's art. I strongly recommend the book as a guide to Copernicus for any reader with a modicum of mathematics.

D. G. KING-HELE

What is Science?

What Is Science For? By Bernard Dixon. Pp. 255. (William Collins: London, July 1973.) £2.50.

THE avowed purpose of this book is to provide "an assessment of what science is and how scientists work". The author is a leading member of a profession that is bound to become more and more important as science becomes more and more complicated and scientific considerations weigh ever more heavily in political decisions. Although the passage is amusing and not unjust, the author is unwise to start off by describing characteristics he most dislikes in a reviewer, because this is asking for retaliatory comments. Perhaps the reviewer specially dislikes an author who chooses as the title of his book a question which (unlike, say, "*was Metternich a negro?*") hardly admits a straightforward answer. But, of course, if the answer had been straightforward there would have been little incentive to write a book.

Dixon starts with an account of the degree of esteem or disfavour in which science has been held from the 17th century to the present day, and he calls attention emphatically but temperately to the activities which have made people see an essential malignancy and have given them a "a new fear of positive evil" in the pursuit of science; he draws a parallel between the bewilderment of

modern scientists at their current revaluation by society and the doubts and bewilderment of the clergy at that reappraisal of their status for which science itself was responsible; but it was ill-judged to use the term "corporate menopause" to describe the condition of the scientific profession today, because there is no evidence that scientific productivity is declining or on the point of giving out. Next: "What is a Scientist?" ... and "is there indeed such a definable figure?" A number of witty case-histories make it clear that scientific activities and the people who carry them out are remarkably diverse. What Dixon says is always pointed and interesting, as a good journalist's writing ought to be, and in spite of occasional pinpricks most scientists will probably regard his account of the matter as a just one. The same goes for his account of what actually goes on in the mind when scientists practise what laymen obstinately believe to be "the" scientific method. So far from being the practitioner of one cut and dried method, he sees the scientist as the practitioner of a certain way of life—a man who by systematic research and occasional imaginative forays but above all by the habit of self-correction builds up interpretations of the world which are ever more trustworthy and reliable and come ever closer to what is called "the truth".

Dixon fully understands and gives due weight to the importance in scientific life of the scientific community, the *internationale* of fellow professionals who scrutinize each others' work, correct it and carry it on. "Scientists of the world unite," Henry Tizard, England's leading scientific administrator, was fond of saying at the end of the Second World War, when it looked as if national rivalry and political ambition between them would do us all in. Actually, we have an *internationale* already but it is a purely professional one and carries no political weight. Thus we shall have to take Lord Zuckerman's advice and become politicians ourselves if we are to influence policy in any effective way. Unfortunately, Dixon's badly overwritten section on research funding with special reference to the Rothschild report illustrates the worst of journalism as clearly as the rest of his book exem-

plifies the best of it, but he has some useful and pointed things to say on "grantsmanship" and how certain non-scientific talents may conduce to getting research support.

Though Dixon disclaimed any intention to write a "scholarly" work he is in fact very well read, intelligent and fair minded and that is the more important part of scholarship anyway. Though scientists come in for some pretty plain speaking, nothing is said that will shake their basic faith in scientific meliorism—the belief that the world has been and may yet be made a better place to live in as a result of scientific research.

P. B. MEDAWAR

Dedicated to Dirac

Aspects of Quantum Theory. Edited by Abdus Salam and E. P. Wigner. Pp. xvi+268. (Cambridge University: London, November 1972.) £7.10; \$23.50.

THIS is not just one of the many *Festschriften* which are now following each other in quick succession as the pioneers of twentieth century physics inexorably reach their sixtieth or seventieth birthday. The editors of this volume, dedicated to Dirac, have spared no effort to make it, not only a fitting tribute to one of the greatest of these pioneers, but a significant contribution, of lasting value, to the history of the heroic period of quantum theory. After a complete bibliography of Dirac's publications, the book opens with three biographical articles. The last of these, by J. Mehra, manages with remarkable psychological insight and literary talent to give a true-to-life picture of Dirac's unique genius and lovable personality; the preceding reminiscences of Van Vleck are, in a lighter vein, quite entertaining and as revealing of the author's as of his hero's character as travellers out of the beaten track in the Rockies and elsewhere. Then comes a sequence of twelve more specialized articles, authoritatively treating of the great problems of quantum theory to which Dirac's name is attached; these contributions are not strictly historical, they offer original views of their eminent authors on the problems in question and their later developments. There would be little point in commenting on them all; each reader will find some of them more to his taste than others. Personally, I found extremely valuable Wigner's considerations on the time-energy uncertainty relation, and thoroughly enjoyed Laurent Schwartz's candid confession of initial scandal when he learned of the "δ-function" and of frightened surprise when he much later saw what the physicists had managed to achieve by manipulations of "distributions"—without being "entitled" to do so by the mathematicians.

L. ROSENFELD

Physics of Atoms

Atomic and Nuclear Physics. By John Yarwood. Pp. 608. (University Tutorial Press: London, 1973.) £3.90.

In recent years it has become the fashion in many university physics courses to introduce atomic and nuclear physics with a large dose of quantum mechanics and in this way to instil some of the difficult theoretical concepts at an early state in an undergraduate's career. Such courses have a great attraction for those with strong mathematical leanings but of necessity the emphasis on theory has relegated the historical and experimental aspects of the subject very much to second place. It is, therefore, interesting to find this new book on atomic and nuclear physics which adopts the unfashionable approach with the emphasis on experiments and on the elementary principles underlying them. Tackling the subject in this way makes rather less demand on the mathematical ability of the reader and yet enables him to familiarize himself with many of the phenomena on the atomic and sub-atomic scale and to learn something of the techniques used in their study.

The first half of the book is concerned with atomic physics which is approached through mass spectroscopy, atomic structure and the elements of wave-mechanics; it also includes chapters on X radiation and atomic magnetism. A very considerable amount of material is covered and the accounts of experiments contain valuable detail which is so often omitted in textbooks. It is perhaps surprising that little mention is made of the photoelectric effect which historically played such an important role in the development of ideas on the particle nature of light, and the sole reference is to the part it plays in the attenuation of an X ray beam. The second and larger half of the book is devoted to nuclear physics which is introduced through natural radioactivity and the properties of radiations. It then proceeds through chapters on particle accelerators, detectors and nuclear fission to nuclear structure, reactions and elementary particles. The strongly experimental flavour is reflected in the considerable space devoted to neutron physics and its application to reactors. Again the coverage is broad and most of the important phenomena of nuclear physics are included and well described.

Although there are several significant errors of physics in the book, this is perhaps hardly surprising in a work which is so wide-ranging. The topics are treated concisely and readably and a wealth of material is contained in this relatively inexpensive book. It is certain that if it were on the shelves of a library it would be used by undergraduates because of the clear and simple way in which the information is laid

out. As a course textbook, however, it is likely to be of most value where quantum mechanics plays little part in the course.

M. A. GRACE

African Gastropods

Sea Shells of Southern Africa—Gastropods. By Brian Kensley. Pp. 225. (Maskew Miller: Cape Town, in collaboration with the South African Museum, 1973.)

SOUTH AFRICAN shores stretch for a distance of well over 2,000 miles and include four climatic zones with the Benguela Current extending cold conditions well up the east coast and the Mocambique and Agulhas Currents on the west bringing semi-tropical conditions as far south as Durban and warming the southern shores. The diversity of the shore populations was fully described in pre-war surveys made by the late Professor T. A. Stephenson.

Although a few shells from South Africa were named by Linnaeus and Lamarck, systematic collection did not begin until the middle of the last century largely by British and United States survey vessels. These were later extended by the Challenger and the Valdivia which trawled and dredged to some depth. Collection by local trawlers had begun by the end of the century.

British conchologists, notably G. B. Sowerby (the third), E. A. Smith and J. R. le B. Tomlin, played a notable part in establishing on a sound basis the taxonomy of South African marine Mollusca. This was followed by the impressive contributions between 1951 and 1964 of K. H. Barnard of the South African Museum.

There have been unfortunate episodes in South African conchology, notably the entirely uncritical *Marine Shells of Port Alfred, South Africa* published by W. H. Turton in 1932. The need for an authoritative and comprehensive account of this most interestingly diverse fauna has long been clear. This task has now been assumed by Brian Kensley of the South African Museum in a volume devoted to gastropods. After an informative introduction, full scope is given to the work of a team of three artists who illustrate, often in colour and invariably with great clarity, all the 900 species.

While I would have welcomed information about habits and habitat, certainty about species is the first essential and both professional and amateur malacologists will welcome this book and look forward to its successor covering the bivalves and other marine molluscs. This is a South African Museum Publication but strangely carries no price nor any indication of the locality of the shore scene depicted on the end papers.

C. M. YONGE

Thermoelectricity

Thermoelectricity in Metals and Alloys. By R. D. Barnard. Pp. x+259. (Taylor and Francis: London, November 1972.) £6.50.

It is more than ten years since the late D. K. C. MacDonald published a splendid monograph on thermoelectricity in metals and alloys. Whilst there have not been any dramatic advances in the subject since then, a new monograph can certainly be justified on the grounds that the intervening period has been one of consolidation. Our understanding of the thermoelectric power of metals is now in a very satisfactory state; in particular, at high temperatures, the dominating influence of the energy dependence of the scattering cross-section (rather than detailed consideration of Fermi surface topology) has led to a unified theory which covers solids, liquids and alloys. Dr Barnard has covered the literature very adequately and his presentation of a mass of new material has ensured that the underlying unity of the subject has been preserved. I was particularly impressed with chapters 4 and 6 which cover a whole range of high temperature effects from a standpoint based on electron scattering. The remaining chapters cover the basic "classical" theory (chapters 1, 2 and 3), the ideas behind the concept of phonon-drag (chapter 5) and a general review of thermoelectricity in metals and alloys, particularly those in which the d-bands materially affect the experimental results.

One criticism: I should have liked to see a little on those cases where the basic formulation is beginning to break down, for example, low density Hg or alloys in which the mean free path is short. This area of condensed matter physics is not well understood and a short account of some of the recent experiments would, I think, round the book off rather nicely.

But, this minor point aside, I found Dr Barnard's book very readable and it will be useful to academic staff and research students who have to lecture on or research into thermoelectricity and its associated phenomena.

J. E. ENDERBY

Classic Ecobotany

Stålfelt's Plant Ecology: Plants, the Soil and Man. Translated by Margaret S. Jarvis and Paul G. Jarvis. Pp. x+592. (Longman: London, December 1972.) £5.50.

THIS translation of the classic treatise on plant ecology by the late Professor Stålfelt, of Lund, has placed in the hands of British ecologists an introduction to an extensive continental literature on the subject. In many respects

Stålfelt was ahead of his time, for he anticipated the development of ecosystem theory and its application to agriculture, forestry and the maintenance of stability in the natural environment.

The emphasis of the book is upon the interaction between plant and soil and it has a distinct bias towards the applied branches of ecology, which is rather refreshing when so many modern texts are exclusively theoretical.

Although the translation reads well, it is sad that more recent work was not incorporated. Of the seven hundred references in the bibliography, only about forty are later than 1960. As a reference text for undergraduate teaching it also suffers the disadvantage of being exclusively botanical when many introductory ecology courses are now integrated botany and zoology. It will provide a useful introduction to plant ecology for undergraduate students of agricultural botany and forestry, although even in its coverage of these fields there is an evident neglect of biotic factors, for example competition and grazing. One wonders whether the translators would have been more profitably employed in writing a new text based on Professor Stålfelt's work.

PETER D. MOORE

African Avifauna

Birds of West Central and Western Africa. By C. W. Mackworth-Praed and C. H. B. Grant. Volume 2. Pp. vi+818+plates 47-93. (Longman: London, April 1973.) £8.

THE surviving author is to be congratulated on the completion of an ambitious project for covering the whole of Africa south of the Sahara with a uniform system of ornithological textbooks. There are three series, each consisting of two volumes, and these deal respectively with eastern and north-eastern Africa, with the southern third of Africa, and with west central and western Africa. There is of course some overlap of species but each series is complete in itself. The first series opened in 1952 and ran into a second edition; the second appeared in 1962-63, and the earlier volume of this series came in 1970. Captain Grant died in 1958, but by then he had put in many years of preparatory study at the British Museum (Natural History) and had laid the foundations, especially as regards taxonomy, of the whole work; he is thus fittingly regarded as joint author even of this final volume.

The area covered by the third series is larger than that usually denoted by the term West Africa, and extends from southern Mauritania to northern Angola, as well as eastwards to the borders of the Sudan, Uganda and Tanzania. This second volume includes all the pas-

serine families except the larks. There are 736 species, some with several recognized races, and each of the latter receives separate treatment. For each, as before, brief particulars are given of distinguishing characters, distribution (with marginal map), habits, nest and eggs, recorded breeding and call. The colour plates figure every species except a few for which drawings have been considered sufficient.

There are some excellent books, of various dates, on the birds of particular parts of Africa; and there are important recent works making a broad biological approach to the whole avifauna. But as a systematic basis for study of the birds of the Ethiopian Region the six volumes of Mackworth-Praed and Grant have no equivalent.

A. LANDSBOROUGH THOMSON

Oxide Films

Oxides and Oxide Films. Edited by John W. Diggle. Volume I. Pp. xiii+537. (Marcel Dekker: New York, November 1972.) \$27.50.

THIS book is the first of a series to be devoted to the general field of the anodic behaviour of materials. The introduction by the editor shows the extent of the aim, which can fairly be described as electrochemical in its bias.

There are to be four volumes on oxides and oxide films, each containing four lengthy reviews of particular topics. The editor acknowledges that some reviews, peripheral to the main topic, will not be electrochemical and one may cite in this area for example "Dielectric Loss Mechanisms in Amorphous Solids" (to appear in volume 2). It does seem unfortunate that the editor has not thought it necessary to find a title of each volume which describes the contents more precisely. The present one is not incorrect but which oxide films? The corrosion films on iron and steel, or the magnetic films used in computer memories, or what?

This first volume opens with an article by V. Brusić on Passivation and Passivity in which passivation phenomena are discussed and the characteristics of the active and passive states are presented. There follows M. J. Dignam's article on Ionic Transport Mechanisms through oxide films. The various mechanisms by which the migration of a charged carrier can occur are studied and applied to chosen problems such as vitreous metal oxides. C. A. Mead has contributed an article on Electronic Current Flow Through Ideal Dielectric Films, relating this to thermionic currents in diodes and in semiconducting and insulating films. The final article, by S. M. Ahmed, is on the Electrical Double Layer at Metal Oxide-Solution Interfaces, presenting an extensive review of published work. Each article

concludes with a very adequate list of references.

This is clearly a book for the specialist, yet there are parts of each article from which the tyro can learn and profit. But, as so often happens today, the price will probably restrict purchases to libraries and to committed research groups. K. J. STANDLEY

Research on Whales

The Sperm Whale. By A. A. Berzin. Translated from Russian. Pp. v+394. (Israel Program for Scientific Information: Jerusalem; Wiley: Chichester, March 1973.) £13.15.

THE sperm whale is the most numerous of the great whales. It contributes about 60% to the world catch of large whales, and nearly half are taken by the USSR. It is also biologically fascinating because of its adaptations to the marine environment. This dual interest led Dr Berzin to assemble his monograph of all the data available on the sperm whale up to 1968. The Soviet whaling fleets in the North Pacific and Antarctic and cruises by research vessels have provided much information which is not widely known to non-Russian scientists, so this critical review of published work and the author's original material is a competent and most welcome survey.

Preferring the specific name *Physeter macrocephalus* L. (1785), Berzin recognizes northern and southern hemisphere sub-species differing slightly in morphometry but not in colour. He covers the osteology of the sperm whale, its digestive, respiratory and urinogenital systems, and with V. M. Malyshev, gives the first full account of the musculature. Recent work on the brain is outlined, and the structure and possible functions of the skin are considered, including the questions of laminar flow and thermoregulation. The curiously formed head of the sperm whale has long intrigued researchers, and recent evidence suggests functions of the nasal passages and spermaceti organ connected with sound production. It is encouraging to find that Berzin states the theories but also expresses reservations where necessary on this and other unproven aspects of the whale's biology.

Research on whales has tended to proceed in parallel in the Soviet Union and outside in recent years, perhaps because of the language problem. This is particularly apparent in the discussion of reproduction and age determination. For example, the author suggests that ovulation in the females is induced, foetal growth is not constant, lactation lasts only one year, and he gives important evidence for believing that two growth layers are formed in the tooth

dentine each year. Opinion elsewhere differs on these subjects, partly because the Soviet results published as long ago as 1961 have not been widely considered. It is good to have a truly critical review of Soviet research available now, and this may help to avoid a repetition of the situation where the slow maturation of the sperm whale testis was described by Berzin in 1963 but recognized independently by other workers some five years later.

Other subjects dealt with are behaviour, and diseases and parasites, including a thorough survey of the helminth fauna by S. L. Delyamure and A. S. Skryabin. Food species, mainly cephalopods, may influence the distribution of sperm whales, and reference is made to the large body of relevant data accumulated in the USSR. There is also an outline of sperm whale catches world-wide, with a useful account of Soviet whaling methods and products.

Our knowledge of sperm whale biology, and reproduction in particular, has advanced since the last of the extensive references quoted was published, but otherwise this excellent translation gives a comprehensive picture of an important international resource.

RAY GAMBELL

Light-Scattering

Light Scattering from Polymer Solutions. Edited by M. B. Huglin. Pp. xviii+885. (Academic: New York and London, August 1972.) £14.50; \$45.

THE method of light-scattering has been applied to physical chemistry of macromolecules in solution owing to the works of P. Debye in 1944 and has seen a successful development in the field of the polymers, synthetic as well as biological. From this time the abundance of literature on this subject has shown the considerable interest of the method for the study of polymer solutions.

There exist a number of reviews giving the main outlines of the theory and the various aspects of this method. A few basic papers more specialized and already published in different journals have been reprinted in one volume in 1964. But the progress in the research of polymers makes necessary a more detailed and modern review on the information obtainable by this method. Consequently the publication of a treatise entirely devoted to scattered light became indispensable. This important book fulfils this purpose. The wish of the editor is "to bridge the gap between the standard book and the papers of an extreme specialization". This new treatise on light-scattering is made up of eighteen chapters; each one, written by an expert,

is self contained without reference to each other.

The topics have been selected by the editor himself. But no chapter is devoted to fundamental bases of the method, except one dealing with "large particle scattering function" $P(\theta)$ which is known to yield important information on the molecular geometry. The essentials of theory are presented, more or less briefly, however, by most of the authors as an introduction to their own subject.

In the beginning of the book, five chapters concern the technology. The first one is devoted to the very important problem of clarifying the solutions. In another chapter, the various apparatuses are described, but, unfortunately, the references being no later than 1966, recent improvements such as the use of laser as light source are hardly mentioned. An important part (150 pages) is reserved for the determination of refractive index increments, which shows its importance; the tabulated data will be very useful for the experimenter.

Among the following chapters treating various problems of polymer solutions, some concern both the synthetic and biological ones. For example, chapter 9 deals with the problems of aggregation or multimerization, chapter 15 with the interactions between polymers and mixed-solvent and chapter 16 with the solutions of polyelectrolytes. But most of them are devoted to synthetic polymers, stereoregular and copolymers. It is worth noting particularly some topics which are untreated elsewhere, such as the influence of various external factors, pressure and temperature; or the effect of electric fields owing to which, beside the standard data, information on the dipolar moment, relaxation time and molecular flexibility is obtainable. The last chapter deals with the early development of the turbidimetric titration, very useful in determining the molecular weight distribution.

Although this book is devoted to "polymers" taken in the broadest sense, and so including biopolymers, the space given to biological topics, around fifty pages, permits only an incomplete view of the possibilities of the method in this field.

The rapid survey of this important volume emphasizes the wealth of information brought by the light-scattering method. But the detailed development of one subject in each chapter and the specialization of each one will make difficult the utilization of the book by anyone encountering the method for the first time. Rather it is suited to polymer scientists, already experienced researchers, for whom it will be an invaluable tool.

J. TONNELAT
S. GUINAND

CORRESPONDENCE

Mercury in Lakes

SIR,—Recently, Aston *et al.*¹ reported that the mercury concentrations within a sediment core from an English lake were highest in the upper layers of sediment. Others^{2,3} have reported similar findings. All have attributed this differential distribution in part to the possibility of increased inputs of mercury with time due to man's activities.

Although there has been some discussion as to the source of this input^{4,5}, a lingering problem involves demonstrating that mercury levels in organisms have become generally elevated. Several researchers⁶⁻⁸ have compared mercury levels in old and recent biological samples and could not document a general increase of mercury content in life forms as time passed. It may be, then, that mercury levels have always been highest in upper sediment layers.

Aquatic organisms can concentrate mercury in their bodies. When they die, sink, and decompose, they would add significant amounts of mercury to the upper sediments. The life cycle of benthic insects offers a particularly striking pathway whereby mercury could be carried upward and ultimately deposited at the sediment-water interface. There is some evidence that tubificid worms could carry substances upward in sediments⁹. Some fish and algae are known to have high mercury loads. Death and decomposition of these organisms would increase the mercury content of upper sediments.

In short, the activity and death of aquatic organisms would continually cycle mercury to the upper sediment layers.

As others have mentioned^{1,2}, several researchers have proposed a geochemical mechanism whereby mercury diffuses upward in sediments. This too may enhance the occurrence of elevated mercury levels in upper sediment layers.

Except in sediments from known mercury contamination areas, the phenomenon that mercury concentrations tend to be highest in upper sediment layers may be a natural condition and not attributable to recent inputs of mercury.

Yours faithfully,

C. S. SIKES
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¹ Aston, S. R., Bruty, D., Chester, R., and Padgham, R. C., *Nature*, **241**, 450 (1973).

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⁷ Barber, R. T., Vijayakumar, A., and Cross, F. A., *Science*, **178**, 636 (1972).

⁸ Kevorkian, J., Cento, D. P., Hyland, J. R., Bagozzi, W. M., and van Hollebeke, E., *J. Pub. Health*, **62**, 504 (1972).

⁹ Brinkhurst, R. O., *USEPA, Ecological Research Series, Project 16010 ECQ*, 68 (1972).

Solar Energy

SIR,—The International Solar Energy Society was formed in 1954 to serve as a centre for information on research and development in the utilization of solar energy. The Society headquarters are in Melbourne, Australia; in countries where sufficient interest exists, national sections of the Society have been established.

At present, there is no British section, although there are nearly enough individual members to allow the formation of one. If such a section were formed it would, by means of newsletters and meetings, bring together British scientists, engineers and environmentalists whose work involves the nature and use of solar energy.

I am assessing the possibility of forming a British section. I should be very grateful to receive any comments, or to send further details of the ISES to anyone who is interested.

Yours faithfully,

M. D. ARCHER

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Obituary

Dr Muriel Robertson

DR MURIEL ROBERTSON, FRS, who died on June 20 at the age of ninety, was educated at Glasgow University, where she graduated as an MA in 1905 and which subsequently awarded her a DSc and, in 1948, an LID. She spent three years as a Carnegie Research Fellow in Ceylon, studying various parasitic Protozoa in the blood of reptiles and fishes. Thus she was introduced to the trypanosomes, a group on which much of her subsequent research was to be done. She discovered and named a trypanosome of a turtle and studied its complete life cycle in both vertebrate

and invertebrate hosts (leeches). This was one of the first life histories of a member of this genus to be elucidated in detail.

Dr Robertson then returned to Britain in 1909 to work for a year as research assistant to Professor E. A. Minchin at the Lister Institute, and subsequently joined the Institute's staff. No doubt it was from Professor Minchin that she acquired much of the cytological expertise she was later so fruitfully to apply to her studies of trypanosomes and other protozoa. In 1911 her wanderlust reasserted itself, and she joined the Royal Society's Sleeping Sickness Commission in Uganda, under Dr

H. L. Duke, as Protozoologist to the Uganda Protectorate. Travel to such relatively unknown regions as central Africa was not commonly undertaken by young ladies in the early years of this century, and Dr Robertson's achievements in this field testify to her adventurous and determined nature, exemplified also perhaps by her use of a bicycle as a means of transport through the forests of southern Uganda.

This period could perhaps be regarded as the acme of her scientific career, when she worked out in detail the entire, complicated developmental cycle undergone by *Trypanosoma gambiense*, the causative organism of human sleeping sick-

ness, which was at that time devastating the population on the northern shore of Lake Victoria. This work, published mainly in the *Proceedings* of the Royal Society, involved cytological studies of extreme delicacy and her beautifully illustrated papers are undoubted classics. Her work on this subject has never been superseded nor indeed equalled, and the accuracy of some of her conclusions (for example, the role of the stumpy blood-stream trypomastigote in infecting the vector, *Glossina* spp.) is only now being fully appreciated.

After this period Dr Robertson returned to the Lister Institute in 1915 as protozoologist, a post which she occupied for the remainder of her working life, which continued until she was at least 78. During the First World War she showed her versatility by making valuable studies, eminently practical at that time, of the anaerobic bacteria causing gas gangrene, and she became secretary of the Medical Research Council's first Anaerobes Committee and a contributor to the Council's System of Bacteriology. Later, she returned to her first scientific loves, the protozoa, continuing her elegant cytological studies on the free living flagellate *Bodo* and on the finer details of nuclear structure and division in *Trypanosoma*. Miss Robertson's practical nature reasserted itself and she began a long series of pioneering studies of the host's immune response to the parasite *Trichomonas foetus*, an economically important cause of bovine abortion. This work was summarized in her contribution to the book *Immunity to Protozoa*, published in 1963 when Miss Robertson was 80. She celebrated her 80th birthday by delivering the sixth Marjory Stephenson Memorial Lecture to the Society for

General Microbiology, in which she discussed the cytology, life cycles and what she referred to as "the highly experimental approach . . . to sex" of her beloved protozoa. In this wide ranging review she showed a wholly typical grasp of modern techniques by referring to electron-microscope observations as well as to her own pioneering researches and to the work of many others, spanning the intervening half-century. Her scientific achievements were recognized by her election to an FRS in 1947.

Everyone who met Dr Robertson was impressed by her kindness, her willingness to impart knowledge, her enthusiasm for her subject and her forthright personality. She belonged to a generation of female scientific explorers which was probably unique. Not only will she be sadly missed by her many friends and her wide circle of scientific acquaintances, but science as a whole will be the poorer for her death. Happily, her great contributions to knowledge remain in the scientific literature and in the work of those whom she advised and inspired.

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Tate and Lyle Limited. Group Research and Development—Annual Report for 1972. Pp. 65. (Reading, Berks: Tate and Lyle Limited, Group Research and Development, 1973.) [105]
University of Oxford. Graduate Studies: Students under Boards of Faculties and Committees as on the first day of Trinity Term 1973. Pp. 227–335. (Oxford: The University, 1973.) 10p. [105]
Department of the Environment. Water Pollution Research Technical Paper No. 13: Mathematical and Hydraulic Modelling of Estuarine Pollution. (Proceedings of a Symposium held at the Water Pollution Research Laboratory, 18th and 19th April, 1972.) Pp. vi+228. (London: HMSO, 1973.) £8.60 net. [105]
Report by the Hydrographer of the Navy 1972. Pp. 38. (NP 130.) (Taunton: Hydrographic Department of the Ministry of Defence, 1973.) [105]
Shoe and Allied Trades Research Association.

Annual Report for 1972. Pp. iv+173. (Kettering, Northants: Shoe and Allied Trades Research Association, 1973.) [155]
BP Statistical Review of the World Oil Industry 1972. Pp. 24. (London: The British Petroleum Company, Ltd., 1973.) [155]
Psychiatrists in Training: The Report of the Royal Medico-Psychological Association's Manpower and Education Project. By Peter Book. (*British Journal of Psychiatry*, Special Publication No. 7.) Pp. xii+163. (Ashford, Kent: Headley Brothers, Ltd., 1973. Published by authority of the Royal College of Psychiatrists.) £2; \$5.35. [155]
Genetic Studies in Mental Subnormality. By B. C. Clare Davison, Peter N. Swift, Philip F. Benson and John D. Studdy. (*British Journal of Psychiatry*, Special Publication No. 8.) Pp. 82. (Ashford, Kent: Headley Brothers, Ltd., 1973. Published by authority of the Royal College of Psychiatrists.) £2; \$5.35. [155]
Natural Environment Research Council. Institute of Geological Sciences. Geomagnetic Bulletin No. 4: Magnetic Results 1970: Eskdalemuir, Hartland and Lerwick Observatories. Pp. ix+154. (London: HMSO, 1973.) £4. [155]
Plastics and the Plastics Industry: a Select Catalogue. Pp. 20. (London: LINK Liaison Office, Central Reference Library, Brixton Oval, SW2, 1973.) *Gratis*. [165]
Department of Trade and Industry. Production and Reserves of Oil and Gas on the United Kingdom Continental Shelf: a Report to Parliament by the Minister for Industry. Pp. 12. (London: HMSO, 1973.) 20p. [165]
The British Food Manufacturing Industries Research Association. Annual Report 1972. Pp. 54. (Leatherhead: The British Food Manufacturing Industries Research Association, 1973.) [165]
Proceedings of the 12th NIAB Crop Conference, 13/15 December 1972: UK Cereal Production after entering the Common Market. Pp. 83. £1. List of Recommended Varieties 1973. Pp. 8. (Cambridge: National Institute of Agricultural Botany, 1973.) [165]
Science Research Council. Daresbury Nuclear Physics Laboratory—Annual Report 1972. Pp. 141. (Daresbury, Nr. Warrington: Daresbury Nuclear Physics Laboratory, 1973.) [165]
Countryside Commission for England and Wales. Countryside Recreation Staff—a Paper for Discussion. Pp. 13. (London: Countryside Commission, 1 Cambridge Gate, Regent's Park, NW1, 1973.) *Gratis*. [165]

Other Countries

CERN—European Organisation for Nuclear Research. CERN—73-4: High Accuracy, Two-Dimensional Read-Out in Multiwire Proportional Chambers. By G. Charpak and F. Sauli. Pp. iii+10. (Geneva: CERN, 1973.) [23]
World Health Organization. Drug Therapy of Cancer. By G. Brule, S. J. Eckhardt, T. C. Hall and A. Winkler. Pp. 163. 20 Sw. francs; £2; \$5. Technical Report Series No. 507: Psychogeriatrics—Report of a WHO Scientific Group. Pp. 48. 4 Sw. francs; 40p; \$1. (Geneva: WHO; London: HMSO, 1972 and 1973.) [23]
US Department of Commerce: National Bureau of Standards. NBS Special Foreign Currency Program in Yugoslavia, 1971–72. By H. Steffen Peiser, Samuel F. Chappell, Emanuel Horowitz, Harvey Yakowitz and Doris Blurbond. (NBS Technical Note No. 753.) Pp. v+65. (Washington, DC: US Department of Commerce, National Bureau of Standards, 1973. For sale by US Government Printing Office.) 90 cents. [23]

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